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August 13, 2004

Divisions of Dockets Management
U.S. Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 2003P-0029
Use of Ozone-Depleting Substances;
Removal of Essential-Use Designations

Dear Sir or Madam:

In the *Federal Register* Notice dated June 16, 2004, for the above captioned matter, the U.S. Food and Drug Administration ("FDA") requested comments on various issues concerning the proposal to remove the essential-use designation for albuterol MDIs.

Enclosed is a report entitled, "Economic Issues Raised in the FDA's Proposed Rule on Removing the Essential-Use Designation for Albuterol MDIs." We prepared this report to assist the FDA in the rulemaking process.

National Economic Research Associates, Inc. ("NERA"), an international firm of economists, was retained by GlaxoSmithKline to analyze the economic issues raised by the FDA in connection with designating albuterol non-essential. Our research represents our independent views on the current and projected market environments for selling albuterol. NERA specializes in applying microeconomics to complex business and legal matters. For over 40 years, NERA economists have contributed to understanding the economic issues in business, legal, regulatory, and public policy forums.

Sincerely,

Richard P. Rozek

RPR:pmb
Enclosure

2003P-0029

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ECONOMIC ISSUES RAISED IN THE FDA'S PROPOSED RULE ON REMOVING THE ESSENTIAL-USE DESIGNATION FOR ALBUTEROL MDIs

by

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Comments submitted to the
U.S. Food and Drug Administration
[Docket No. 2003 P-0029]

August 13, 2004

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Economic Issues Raised in the FDA's Proposed Rule on Removing the Essential-Use Designation for Albuterol MDIs

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I. INTRODUCTION

The U.S. Food and Drug Administration ("FDA") initiated a rulemaking "to amend its regulation on the use of ozone-depleting substances ("ODSs") in self-pressurized containers to remove the essential-use designations for albuterol used in oral pressurized metered-dose inhalers ("MDIs")."[1] The FDA has "tentatively concluded that [after the policy change] patients will be adequately served by albuterol HFA [hydrofluoroalkane] MDIs within the timeframes discussed in [the Notice]."[2] The FDA has also observed that implementing the policy change will facilitate a controlled transition to an albuterol chlorofluorocarbons ("CFC")-free world, reduce adverse health consequences of ultraviolet-B radiation, signal the interests of the U.S. in complying with international agreements, and provide appropriate incentives to conduct research and development ("R&D") in the pharmaceutical industry.[3]

While recognizing the benefits resulting from removing the essential-use designation for albuterol MDIs, the FDA has requested comments on several economic issues related to the

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* The authors are Senior Vice President and Senior Analyst, respectively, at National Economic Research Associates, Inc. ("NERA"). GlaxoSmithKline ("GSK") provided financial support for the economic research described in this report.

1 Department of Health and Human Services, FDA, 21 CFR Part 2, Docket No. 2003P-0029, RIN 0910-AF18, "Use of Ozone-Depleting Substances; Removal of Essential-Use Designations," *Federal Register*, Vol. 69, No. 115, June 16, 2004 ("Notice"), p. 33602. In this report, we refer to removing the essential-use designation for albuterol MDIs as the policy change. Albuterol MDIs are used as a rescue medication for treating asthma and chronic obstructive pulmonary disease ("COPD").

2 Notice, p. 33608.

3 Notice, pp. 33614-5.

marketplace for albuterol MDIs before and after the policy change. We submit this report to provide information on these economic issues. Specifically, we:

- Summarize our previous submission to FDA Docket No. 03P-0029[4] regarding the economic impact on patients and third-party payers in the first year after the policy change. Given existing and proposed marketplace characteristics, our results are a worst-case estimate of the impact. We also revise our calculation of the impact on patients with insurance to reflect new information on the relationship between the magnitude of co-payments and use of certain pharmaceutical products.
- Compare the analysis in our previous submission with the analysis presented in the Notice.
- Correct an inaccurate statement in the Notice that "higher prices may reduce the MDIs sold by between 400,000 and 1 million per year..."[5] This range overstates any adverse impact of the policy change for at least four reasons. First, our analysis of sales of albuterol MDIs from 1992 to the present reveals that usage remained relatively constant at approximately 50 million MDIs annually, despite the entry of lower-priced, generic albuterol MDI products. Second, the product characteristics of albuterol MDIs suggest that the demand is inelastic or insensitive to changes in price. Third, the Notice does not account for public and private sector patient assistance and discount programs that provide albuterol HFA MDIs for free or at reduced prices. Fourth, insurers have the incentive to avoid emergency room visits or other costly medical care for asthma and COPD patients by keeping co-payments for albuterol MDIs low. These characteristics suggest that the policy change is unlikely to cause any

[4] Richard P. Rozek and Emily R. Bishko, "The Impact on Patients and Payers of Designating Albuterol a Non-Essential Use of an Ozone Depleting Substance," National Economic Research Associates, Inc., September 8, 2003. Our previous submission is cited as Reference 8 in the Notice. See Notice, p. 33618.

[5] Notice, p. 33617. The calculation in the Notice is 360,000 MDIs, which is rounded upward to 400,000 MDIs. Notice, p. 33615.

material impact on either total demand for albuterol MDIs or patient access to albuterol MDIs.

- Correct another inaccurate statement in the Notice that "[t]he proposed rule could result in increased health expenditures of about a billion dollars for each year between the reintroduction of generic competition in this market and the selected year for removing the essential-use designation."[6] This inaccuracy is primarily due to two factors. First, the Notice overstates the price difference between the brand and generic versions of albuterol MDIs borne by patients. Second, the Notice adopts a static, rather than dynamic, view of the marketplace for selling albuterol MDIs. The Notice did not take into account the effects of the existing and expected marketplace characteristics that benefit asthma and COPD patients, and promote access to albuterol MDIs.

- Discuss the economic conditions that suggest that the two existing suppliers of albuterol HFA MDIs are likely to compete after the policy change. For example, the threat of entry by additional sellers of albuterol in non-ODS delivery systems, competition from other products both currently available and in the R&D pipeline for treating asthma or COPD, and the increasing ability of certain public and private sector buyers to exert buyer power benefit patients who use albuterol MDIs.

- Describe the effects of proposals by GSK to distribute free samples of Ventolin® HFA (a brand albuterol MDI product) through its sales representatives to physicians, continue sponsoring patient assistance programs, provide discount "Ventolin HFA Savings Checks" (coupons)[7] to patients throughout the U.S., and freeze the wholesale price of Ventolin® HFA on reducing the cost of the policy change to the overall healthcare system. Most notably, GSK's commitments along with other patient assistance programs and the underlying structure of the

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[6] Notice, p. 33617.

[7] See "Comments on June 16, 2004 FDA Proposed Rule to Remove Essential Use Designation for Albuterol Metered-Dose Inhalers Containing Chlorofluorocarbons (FDA Docket 03P-0029) Submitted by GlaxoSmithKline" ("GSK Comments"), Section 2.2.

marketplace alleviate concerns about access to albuterol MDIs by the potentially vulnerable low-income, uninsured patient population.

We conclude that the economic evidence supports a near-term effective date for removing the essential-use designation for albuterol MDIs. All patients will continue to be adequately served after the policy change. In that regard, the FDA should adopt December 31, 2005 as the effective date for the policy change. We found no economic factors to support any other date.

II. PREVIOUS SUBMISSION

A. Summary of Results

In our previous submission, we focused on the economic issues surrounding whether patients will be adequately served after the FDA designates albuterol MDIs non-essential. Specifically, we analyzed the cost impact on patients and third-party payers to determine whether patients would have access to albuterol MDIs in the first year after the policy change. We prepared a worst-case analysis in which we identified the patients, third-party payers, and government programs that would incur higher average prices for albuterol MDIs in the first year after the policy change. As we noted in our previous submission, but did not quantify, there are institutional characteristics in the marketplace that will alleviate any material adverse impact on patients and third-party payers (private and government). These characteristics include additional product samples; public and private patient assistance and discount programs; greater information available to patients, physician, and payers about these programs; buyer power; insurance coverage of outpatient prescription pharmaceuticals for Medicare enrollees;[8] competition between sellers of the existing albuterol HFA MDI products (Proventil® HFA and Ventolin® HFA); and entry by sellers with new versions of albuterol in non-ODS delivery systems.

[8] A provision in the Medicare Prescription Drug, Improvement and Modernization Act of 2003 provides people eligible for Medicare with an entitlement to coverage for outpatient prescription pharmaceuticals beginning in 2006.

In preparing our original analysis, we examined public data on the pharmaceutical industry generally and data on albuterol MDIs specifically. Information on general pharmaceutical industry trends does not constitute a sufficient basis to analyze the effects of the policy change with regard to albuterol MDIs. The general information on the pharmaceutical industry is useful for understanding the complex vertical structure through which products such as albuterol MDIs move from manufacturers to patients.[9] For our quantitative analysis, we relied on detailed, product-specific data from IMS Retail Perspective®/Provider Perspective® on the use of albuterol MDIs.[10] We identified the share of albuterol MDIs sold through four groups: Retail, Clinics/Universities/HMOs, Non-Federal Hospitals, and Federal Facilities. Within the Retail group, we further identified three types of patients: Cash, Insurance, and Medicaid.[11] See Exhibit 1. We observed that total use of albuterol has remained relatively stable from 1992 to the present at approximately 50 million MDIs annually even though the U.S. population grew and generic entry occurred during this period. See Exhibit 2.

In our previous analysis, we made several simplifying assumptions regarding the marketplace for selling albuterol MDIs including the following:

- no additional samples,
- no manufacturer rebates to government programs such as Medicaid above the legally mandated minimum,
- no market entry beyond the two existing albuterol HFA MDI products,
- no discounts to other payers above current levels for HFA MDIs,
- no additional price competition for the HFA MDI products, and

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[9] In a few cases, pharmaceutical products may be distributed to patients outside this typical vertical structure. For example, some patients obtain samples of albuterol MDIs directly from physicians.

[10] Other data sources we relied on include Verispan, National Association of Chain Drug Stores, American Lung Association, and the U.S. Census Bureau.

[11] IMS reports sales through 13 channels: chain stores, clinics, federal facilities, food stores, health maintenance organizations (HMOs), home healthcare, independent, long-term care, miscellaneous (other), prisons, universities, mail order, and non-federal hospitals. For ease of analysis, we combined these channels into four groups based on the magnitude of the average prices paid by members of the group according to IMS, and whether the channels through which albuterol products sold for relatively low prices contained public or private institutions. See our previous submission, p. 13.

- higher average co-payments charged to patients with private insurance for brand products than for generic products.

Under these assumptions, we calculated the increase in costs to patients per albuterol MDI for the four groups. Specifically, patients obtaining albuterol through the two components of the Retail group—Retail-Cash and Retail-Private Insurance—would incur increases of $8.61 and $10.57 per MDI, respectively. Patients obtaining albuterol MDIs through the remaining Retail component (Retail-Medicaid) and the other three groups (Clinics/Universities/HMOs, Non-Federal Hospitals, and Federal Facilities) would incur no change in costs from their current situations.

Using the annual volume of 50 million albuterol MDIs, we estimated that the average price of an albuterol MDI for all payers (patients and third-party), across all four groups, and all forms (generic and brand, CFC and HFA) would increase by $9.87 in the first year after the policy change. Our worst-case estimate is an overall increase in costs to the healthcare system of approximately $494 million for the first year after the policy change. The average increase borne by patients out-of-pocket would be $7.33 per MDI. Third-party payers (public and private) would incur an average increase of $2.54 per MDI. On a daily basis, the total cost increase would be 0.5¢ per capita or 4.4¢ per currently diagnosed asthma or COPD patient. Alternatively, the average increase in costs in the first year would be $1.69 per capita or $16.02 per asthma/COPD patient. Based on the historical stable market demand, the use of albuterol as a rescue medication, and the relatively low market price per prescription,[12] cost increases to patients and third-party payers of these magnitudes are unlikely to have a material effect on future use of albuterol MDIs.

[12] The average price of a prescription for a brand pharmaceutical product in 2003 was $83.66, which is more than twice the cost for a prescription of Ventolin® HFA in 2003. "Industry Statistics, Industry Facts-at-a-Glance, Pharmaceutical Pricing," National Association of Chain Drug Stores, http://www.nacds.org/wmspage.cfm?parm1=507.

B. Identical Co-Payments for Brand and Generic Products

Recent work by Goldman et al.[13] addresses the effects on insured patients of increasing co-payments for certain pharmaceutical products including products for treating asthma. Goldman et al. presents evidence that patients who forego using some relatively low cost pharmaceutical therapies for asthma due to increased co-payments may ultimately incur higher healthcare costs for emergency room visits and hospital stays. There is an important policy implication, which is not addressed in the Notice, for insurers from this research. Currently, insurers often use a tiered co-payment structure based on whether a pharmaceutical product is a brand or generic product irrespective of the disease the product treats. To avoid higher healthcare costs, insurers should consider adopting a differential co-payment structure with lower co-payments for diseases where foregoing low cost medicines leads to consuming more expensive healthcare services. Based on the results from Goldman et al., co-payments for brand pharmaceutical products to treat asthma and diabetes should be kept relatively low when no generic alternatives exist.[14]

The significance of these results for our model is that, rather than assume the co-payment for brand products remains at $22 per prescription after the policy change, private insurers should reduce the average co-payment for Proventil® HFA and Ventolin® HFA to $10, the average co-payment for a generic product, as a means of maintaining the incentives for asthma and COPD patients to purchase albuterol HFA MDIs to avoid the higher costs associated with emergency room visits and hospital stays. We incorporated this approach to co-payments as an assumption in our model; that is, insurers reduce the co-payment for Proventil® HFA and Ventolin® HFA after the policy change to $10. Under this assumption, the

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[13] Dana P. Goldman, Geoffrey F. Joyce, Jose J. Escarce, Jennifer E. Pace, Matthew D. Solomon, Marianne Laouri, Pamela B. Landsman, and Steven M. Teutsch, "Pharmacy Benefits and the Use of Drugs by the Chronically Ill," *Journal of the American Medical Association*, Vol. 291, No. 19, May 19, 2004, pp. 2344-2350. This article is cited as Reference 2 in the Notice. See Notice, p. 33617.

[14] A recent study of employees at Pitney Bowes revealed that "employees with asthma, diabetes, depression or hypertension who weren't taking their medicine regularly were also at risk for becoming big spenders [or high cost claimants]...To get employees with common chronic illnesses to take their meds,...[t]hey did away with the three-tiered pricing structure for drugs used to treat asthma, diabetes and hypertension. Instead of making employees kick in up to half the cost for brand-name drugs, Pitney Bowes would provide all asthma, diabetes and hypertension drugs at the generic rate of 10 percent....The median cost of care for employees with asthma decreased 15 percent in 2002, while costs for diabetes patients fell 12 percent." Alice Dragoon, "An Ounce of Prediction," *CIO*, July 1, 2004, pp. 81-2.

impact of the policy change is to reduce the average cost per albuterol MDI for a patient with private insurance by $1.43 since the patients currently paying co-payments of $22 would now pay $10 after the policy change. All the other results remain the same.

III. CRITIQUE OF THE ANALYSIS PRESENTED IN THE NOTICE

A. Analysis in the Notice

The Notice contains an estimate of the increase in consumer expenditures for albuterol MDIs due to the policy change in present value terms (2006) of between $6.9 billion and $7.9 billion depending on whether the discount rate is 7 percent or 3 percent, respectively.[15] According to the Notice, the later the effective date for implementing the policy change, the lower the increase in consumer expenditures due to the timing of generic entry for albuterol HFA MDIs. The increase in consumer expenditures calculated in the Notice is zero if the policy change is not implemented until generic albuterol HFA MDIs are available.[16] Further, the Notice estimates that up to 1 million albuterol MDIs may not be purchased annually as a result of the higher average price for albuterol MDIs after the policy change.[17] Specifically, the Notice claims that:

- "[t]hese estimates are based on a current retail price difference of approximately $23 between branded and generic albuterol CFC MDIs"[18] that remains constant throughout the period under review (e.g., until generic HFA products enter the market);

[15] Notice, pp. 33610-1. The analysis in the Notice takes into account that some payers will not be affected by the policy change. Consumers who are purchasing the brand version of albuterol MDIs before the policy change will not be adversely affected by the change. They will still be able to purchase the brand HFA MDIs at the same price as the brand CFC or HFA MDIs since the brand products in CFC or HFA MDIs are sold at approximately the same price.

[16] Notice, pp. 33611-2.

[17] Notice, p. 33610.

[18] Notice, p. 33610.

- there will be no competition until either 2010 or 2015, the likely dates for entry by generic versions of albuterol HFA MDIs based on patent expiration for the patents governing the existing albuterol HFA MDI products; and[19]
- the effect of a higher price could potentially reduce the use of albuterol by "400,000 to 1 million MDIs per year."[20]

These inaccurate views result in estimates that substantially overstate the cost of the policy change. They lead to conclusions that are in contrast to the results we presented in our previous submission.

B. Comparison of Our Previous Submission and the Notice

1. Estimates of the Cost Impact on Patients

The analysis presented in the Notice uses data that focuses on the change in revenues to retailers, not the change in costs to patients. Specifically, the price differential of $23 is calculated using data obtained from the IMS National Prescription Audit *Plus*® ("NPA Plus") database for first quarter in 2004.[21] We understand that these data measure total revenues received by a pharmacy from patients and third-party payers. For example, they include both patient co-payments and insurer payments. Multiplying the change in retailer revenue by number of units does not measure change in consumer expenditures; that is, it is not a measure of the impact on patients. The Notice incorrectly characterizes these data as representing "consumer expenditures."[22]

In addition, the NPA Plus represents sales through selected retail channels only. Measuring differentials in brand and generic prices through the Retail group only and applying the differentials to all generic purchases through Retail and Non-Retail groups (Clinics/Universities/HMOs, Non-Federal Hospitals, and Federal Facilities) overstates the

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[19] Notice, pp. 33610. "Thus, lower priced generic versions of albuterol HFA MDIs can be expected to be marketed as early as 2010, or as late as 2015 depending on the validity of the patents involved." Notice, p. 33608.

[20] Notice, p. 33610.

[21] Notice, p. 33610. Data from NPA Plus are proprietary to IMS HEALTH.

[22] Notice, p. 33610.

impact to the extent that certain buyers can negotiate lower prices. Further, the data relied on by the Notice excludes retail channels such as the Internet, mail order, and long-term care pharmacies.[23] Finally, the Notice relies on NPA Plus data from the first quarter in 2004.[24] Relying on data from one quarter does not capture the extent to which pharmaceutical prices fluctuate within a year.[25]

In our previous submission, we calculated the average increase in costs borne by patients and third-party payers across four groups (Retail, Clinics/Universities/HMOs, Non-Federal Hospitals, and Federal Facilities) to be $9.87 by analyzing the actual acquisition costs and associated mark-ups for brand and generic products in the specific groups through which albuterol MDIs are distributed to patients. Our average prices before the policy change reflect both brand (CFC and HFA) and generic albuterol MDI products being sold, and the price after the policy change measures only brand albuterol HFA MDI products. In analyzing the groups separately, we determined the average amount of the cost increase that patients and third-party payers incur to be $7.33 and $2.54, respectively.

We relied on data for two full years on sales of albuterol MDIs from the IMS Retail Perspective®/Provider Perspective®, which represents transactions from the wholesaler to retailer and other sellers (e.g., hospitals and clinics).[26] For the Retail Group, we then applied an appropriate mark-up to determine the price charged at retailers by type of payer and type of product (brand or generic).[27] Retailers generally apply a lower mark-up to brand products compared to generic products. In contrast to the $23 differential in the analysis presented in the Notice,[28] we found that the difference in total price between brand and generic albuterol MDIs

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[23] Department of Health and Human Services, FDA, Center for Drug Evaluation and Research, Pulmonary-Allergy Drugs Advisory Committee Meeting ("PADAC Meeting") Transcript, June 10, 2004, p. 70. The NPA Plus data excludes Internet and mail order pharmacies. The Notice additionally excluded long-term care pharmacies.

[24] Notice, p. 33610.

[25] Asthma is a disease that has seasonal tendencies. See http://asthma.about.com/cs/seasonalasthma.

[26] Data from this database are proprietary to IMS HEALTH.

[27] We analyzed albuterol distributed through non-retail channels separately.

[28] Notice, p. 33610.

at the retail pharmacy level to be $8.22, $11.68, and $15.54 depending on whether the patient was in the Retail-Cash, Retail-Private Insurance, or Retail-Medicaid category, respectively.[29]

2. Estimates of Reduced Demand for Albuterol MDIs

The Notice raises a concern that after the policy change "the higher prices [of brand albuterol HFA MDIs] will discourage some people from buying albuterol."[30] This view is in contrast to the statement in the Notice that "[t]he best evidence available to us indicates that the demand for prescription drugs is generally quite inelastic with respect to price changes, so even this relatively large price increase is likely to cause changes in the consumption of MDIs that are quite small relative to the market."[31]

Beginning with 40 million albuterol MDIs as the current level of generic usage, the Notice estimates that 44.4 million generic albuterol MDIs would be sold in 2014 absent the policy change. Assuming generic entry occurs in 2015 and a discount rate of 7 percent, the Notice estimates that the present value of the increased expenditures of albuterol in 2014 is $600 million since consumers would pay a higher price for brand albuterol MDIs than the price of generic albuterol MDIs.[32]

As described above, the Notice also estimates that there may be a possible reduction in use of albuterol MDIs of 400,000 to 1 million in 2006 "due to the price increase associated with the loss of cheaper generic competition."[33] Given these estimates, it is inaccurate to measure increased expenditures for albuterol MDIs without first subtracting the estimated reduction of

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[29] For each group of channels, we determined the average impact to patients and third-party payers by calculating the difference between the current average cost of brand (CFC and HFA) and generic albuterol MDIs times the number of units sold through the applicable channels from the expected cost of albuterol HFA MDIs after the policy change (based on the current brand HFA MDI price) times the total number of HFA units sold after the policy change (50 million albuterol MDIs). Through each group of channels, we determined the applicable share of cost borne by patients. For example, cash payers incur the entire change in cost whereas patients with insurance incur co-payments of $22 and $10 for brand and generic albuterol MDIs, respectively. The result is that patients in the Cash and Private Insurance categories would incur an average increase of $8.61 and $10.57 per MDI, respectively, due to the policy change. See Tables A-1 to A-6 in the Appendix to our previous submission. The Appendix is attached to this report.

[30] Notice, p. 33609.

[31] Notice, p. 33607.

[32] Notice, p. 33611.

[33] Notice, p. 33610.

400,000 to 1 million MDIs that are also due to the higher price. The Notice does not appear to take this into account. The "major quantifiable effects of"[34] the policy change identified in Tables 2 and 3 of the Notice are overstated.

Our worst-case analysis was for the first year after the policy change. We noted that there are institutional factors that will alleviate the impact. The analysis in the Notice takes a static view that nothing will change in terms of the competitive environment until generic competition emerges for the two existing albuterol HFA MDI products in 2010 or 2015. Dynamic factors including GSK's proposed sampling and coupon initiatives, public and private patient assistance and discount programs, competitive discipline from insurers (public and private) able to control product usage through formularies or other means, renewed competition between the existing sellers of albuterol HFA MDIs, competition from other non-ODS albuterol products, and introduction of new treatments for asthma and COPD will alleviate or mitigate the impact of the policy change over time on prices for albuterol MDIs.

3. Year-to-Year Fluctuation in Sales of Albuterol MDIs

It is helpful to view the concern expressed in the Notice that 400,000 to 1 million fewer MDIs may be sold to patients after the policy change in light of the year-to-year fluctuations in sales of albuterol MDIs that occurred in the past. Based on IMS data on sales of MDIs from 1992 through 2004 (annualized), there were 12 observations of year-to-year volume changes. The year-to-year change (either positive or negative) exceeded 1 million albuterol MDIs for 10 of the 12 observations. See Exhibit 3. Use of albuterol MDIs fluctuating by 1 million or more is commonplace. We observed that total sales of albuterol MDIs in 1999 were 51.0 million MDIs, but 3.5 million fewer albuterol MDIs were sold in 2000. In 2001, there were 48.0 million albuterol MDIs sold, but 2.3 million fewer MDIs were sold in 2002. As these examples illustrate, there may be decreases of 1 million or more albuterol MDIs in a given year even though generic versions of albuterol CFC MDIs are available.

[34] Notice, p. 33611-2.

IV. EFFECTIVE COMPETITION

One issue raised at the PADAC Meeting concerned the number of sellers that "make a difference on price."[35] Theoretical and empirical research in economics as well as economic evidence from the pharmaceutical and other industries suggests that the two albuterol HFA MDI products that will be available to asthma and COPD patients after the policy change will allow these patients to reap the benefits of competition.

A. Choices Currently Available to Patients and Physicians

Albuterol is a rescue medication that has been available in the U.S. since 1981. Generic versions have been available since 1995. In 2004, there are only three sellers of albuterol MDIs with non-trivial market shares. See Exhibit 4. Other inhaler products exist that contain albuterol; for example, Combivent® (ipratropium bromide and albuterol sulfate), a treatment for COPD, will not be affected by the current rulemaking.[36] These products will still be available to patients. If the FDA removes albuterol CFC MDI products from the list of essential uses on December 31, 2005, there will be at least two competing products available to consumers. Given the existing approved albuterol HFA MDIs and the potential competition from other albuterol products, there will viable choices available to patients and physicians.

Therapeutic competition frequently occurs among pharmaceutical products. "Other drugs are often a larger threat to a given patented drug than the generic entry it may face down the line when the patent expires."[37] Therapeutic competition in treating asthma or COPD exists as well. Better maintenance medications have been introduced to forestall or reduce the need for albuterol MDIs. The Uniform System of Classification ("USC") codes for asthma and COPD include all medications for respiratory therapy generally (USC 28000), beta agonists (USC 28110), and beta agonists aerosol (USC 28111). The *Physicians' Desk Reference* ("PDR") lists 40 products for treating asthma or COPD. See Exhibit 5. Physicians and patients

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[35] PADAC Meeting Transcript, p. 252.

[36] Notice, p. 33605.

[37] Frank R. Lichtenberg and Tomas J. Philipson, "The Dual Effects of Intellectual Property Regulations: Within- and Between-Patent Competition in the U.S. Pharmaceuticals Industry," National Bureau of Economic Research, Working Paper 9303, October 2002, p. 5

currently have choices for treating asthma and COPD, which will not be affected by the policy change except that albuterol CFC MDIs will not be available.

B. Products in Development for Asthma and COPD

The FDA has already approved two versions of albuterol HFA MDIs (Proventil® HFA and Ventolin® HFA).[38] It has also concluded that two such products being available to consumers support proceeding with the current rulemaking. A concern may be whether two competing albuterol HFA MDI products will create sufficient competition after the policy change eliminates the albuterol CFC MDIs from commercial sale.[39] As discussed below, two sellers can be sufficient for competition in pharmaceutical markets especially when there is a threat of entry into this pharmaceutical category from additional therapeutic competitors. Existing sellers will compete aggressively. The existing sellers will attempt to expand their presence among patients, reputations with physicians, access to formularies etc.

New and improved products have been introduced, and R&D is ongoing to find even more treatments for asthma and COPD. The Pharmaceutical Research and Manufacturers of America ("PhRMA") recently published "New Medicines in Development for Asthma and COPD".[40] There are 47 products in various stages of development from Phase I through New Drug Applications ("NDAs") submitted to the FDA. Six of the products are identified as having NDAs submitted to the FDA. Of the six, two are for albuterol or levalbuterol products (Volare® and Xopenex® MDI). See Exhibit 6.

As patients adjust to the policy change, they will have to discuss the existing and new treatment options with their physicians. Stimulating dialogue between patients and physicians will likely help patients evaluate the available options and select the best course of therapy for their specific medical problems. This benefit of improved patient/physician dialogue is not addressed in the Notice.

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[38] The FDA approved Proventil® HFA and Ventolin® HFA in 1996 and 2001, respectively. FDA, Center for Drug Evaluation and Research, *Electronic Orange Book*.

[39] PADAC Transcript, pp. 252-256.

[40] "New Medicines in Development for Asthma and COPD," PhRMA web site, August 6, 2004.

C. Two Sellers Likely to Create Sufficient Competition

1. Pharmaceutical Examples

a. Albuterol CFC MDIs

There is evidence that suggests competition exists when only two brand pharmaceutical products with identical active ingredients, delivery systems, and indications are available to patients in the U.S. From 1981 to 1995, Schering and GSK competed by selling the brand albuterol CFC MDI products Proventil® and Ventolin®, respectively. During this period, the two sellers competed aggressively for sales in terms of price and services provided to patients, physicians, pharmacists, and payers. We examined IMS data on dollar sales for these two products for the period January 1992 through December 1995 (when generic versions of albuterol MDIs entered).[41] We found that the share of dollar sales for each seller was approximately 50 percent, which indicates there was no dominant seller. The individual shares of Schering and GSK fluctuated suggesting that the sellers were competing.[42] See Exhibit 7. GSK's share of albuterol MDI sales has been small and declining since generic competition emerged in 1995. More recently, GSK withdrew Ventolin® CFC MDIs from commercial sale. After the policy change, Schering and GSK will likely renew their rivalry when selling Proventil® HFA and Ventolin® HFA, respectively.

b. Other Pharmaceutical Products

Similarly, we analyzed three other examples when two brand pharmaceutical products with the same active ingredient and delivery systems, and similar indications were available commercially in the U.S.:

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[41] These data were the only data available from a period of time without generic albuterol MDIs.

[42] "One plausible interpretation of the instability and turnover measures is that greater instability or turnover indicates a greater chance for competitive results." John M. Vernon, *Market Structure and Industrial Performance: A Review of Statistical Findings*, Allyn and Bacon, Inc., 1972, p. 46. "[A] churning among competing firms, as reflected by market share instability, may suggest active rivalry." Ralph D. Sandler, "Market Share Instability in Commercial Airline Markets and the Impact of Deregulation," *Journal of Industrial Economics*, Vol. 36, No. 3, March 1988, p. 328. The results of another study "lend support to the view that market share instability is a symptom of ineffective collusion." Robert W. Staiger and Frank A. Wollak, "Collusive Pricing with Capacity Constraints in the Presence of Demand Uncertainty," *Rand Journal of Economics*, Vol. 23, No.2, Summer 1992, p. 203.

- Intron®-A and Roferon®-A;
- Prinivil® and Zestril®; and
- Beconase® and Vancenase®.

We reviewed historical data from IMS on dollar sales and calculated each product's share of dollar sales relative to the total dollar sales for the pair of products for a period of at least five years. In each case, the fluctuating shares of dollar sales for two brand products suggest competition during the applicable period. For example, Intron®-A was the first interferon alfa product available in the U.S. Intron®-A (interferon alfa-2b) captured 100 percent of the share of dollar sales. In July 1986, Roferon®-A (interferon alfa-2a) was launched. Within eight months, each product sold approximately 50 percent of the total dollars sales. Over the subsequent five years, the shares of each product fluctuated over time, which suggests the rivalry between the two products continued. The shares of each seller fluctuated over time, but generally remained between 40 and 60 percent of dollar sales until 1991.[43] See Exhibit 8. Combined dollar sales of the two products grew over the period 1987 through 1991 at a compound annual growth rate of 35 percent.

We observed similar patterns for the other two product pairs. The two lisinopril products Prinivil® and Zestril® were launched in December 1987 and January 1988, respectively, as treatments for congestive heart failure, hypertension, and myocardial infarction. By the middle of 1988, Zestril® surpassed Prinivil® in terms of share of dollar sales. The two sellers competed so that their respective shares fluctuated over time, but remained between 40 and 60 percent. See Exhibit 9. Combined dollar sales of the two products grew over the period 1988 through 1993 at a compound annual growth rate of 57 percent.

Beconase® and Vancenase® were two versions of beclomethasone dipropionate that began competing in 1981. Initially, the share of Vancenase® exceeded that for Beconase®. Within two years of launch, Beconase® achieved approximately 50 percent of dollar sales. The shares of the two sellers fluctuated due to competition, but each seller maintained about 50

[43] Two sellers with approximately an equal share of dollar sales represent a more competitive market structure than one dominant seller with 70 percent of the sales and a fringe of smaller sellers with five percent shares of sales. See the discussion of the Herfindahl-Hirschman Index as a measure of market competition in our previous submission (p. 22).

percent of the total dollar sales. See Exhibit 10. Combined dollar sales dollar sales of the two products grew over the period 1982 through 1986 at a compound annual growth rate of 29 percent.[44]

2. Economic Literature and Examples

a. Theory and Empirical Studies

Assessing competition in markets often begins by examining the number and size of the sellers. The economic literature contains both theoretical and empirical studies on market environments with few sellers where competition among the sellers is sufficient to produce prices at competitive levels. With two competitors, one classic view in economic theory regarding price competition between the two rivals selling homogeneous products is that one seller reduces its price to increase its share of sales. The other seller then offers a lower price to avoid losing sales. The price-cutting continues until the market price reaches the competitive level.[45] Empirical work by John Kwoka found that equality of size among the largest firms in a market often provides sufficient rivalry to stimulate competitive market performance.[46]

Experimental economics is another area in which economists can study the behavior of market participants under various controlled or laboratory trading conditions. A general conclusion of this literature is that experimental markets produce price competition with relatively few (two or more) sellers. One recent set of results with two sellers reported non-collusive outcomes in two-thirds of the experiments.[47] In experimental trading situations in

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[44] The nature of competition in pharmaceutical markets is often influenced by the sophisticated buyers such as the federal facilities, Medicaid, or HMOs with the ability to move market share can induce competitive outcomes with two sellers. The competitive discipline provided by sophisticated buyers benefits other buyers in a market.

[45] Peter Asch, *Economic Theory and the Antitrust Dilemma*, John Wiley & Sons, Inc., 1970, pp. 58-59. In the pharmaceutical industry, the price cutting could take the form of one seller offering greater discounts or rebates on its product.

[46] John E. Kwoka, Jr., "The Effect of Market Share Distribution on Industry Performance," *Review of Economics and Statistics*, Vol. 61, No. 1, February 1979, pp. 101-109; and John E. Kwoka, Jr., "Does the Choice of Concentration Measure Really Matter?" *The Journal of Industrial Economics*, Vol. 29, No. 4, June 1981, pp. 445 - 453.

[47] Steffen Huck, Hans-Theo Normann, and Jorg Oechssler, "Two Are Few and Four are Many: Number Effects in Experimental Oligopolies," *Journal of Economic Behavior & Organization*, Vol. 53, 2004, pp. 435-446. See also Charles A. Holt, "Industrial Organization: A Survey of Laboratory Research," Chapter 6 in *The*

which both buyers and sellers are active market participants, buyers often discipline even two sellers by their aggressive behavior.

b. Examples from Other Industries

Experience in other industries has revealed that two sellers may be sufficient for competition. For example, the U.S. Federal Trade Commission ("FTC") approved the merger of The Boeing Company and McDonnell Douglas Corporation, two of the three firms that competed in the large (over 80 passenger) commercial airline market. Since the merger in 1997,[48] the choices for buyers have been Boeing and Airbus Industrie. The FTC staff interviewed over 40 airlines (buyers of commercial aircraft) before the Commission reached the decision to approve the merger.[49] The absence of complaints from buyers is often a major factor in approving mergers when the underlying market has few competitors.

A second example is cellular telephone competition. The U.S. Federal Communications Commission ("FCC") began licensing commercial cellular service providers in 1981 and completed licensing the majority of operators by 1992. The FCC divided the U.S. and its possessions into 734 cellular market areas. Two facilities-based cellular systems were licensed in each market area.[50] The FCC allocated 50 megahertz of spectrum in the 800 MHz frequency band for the two competing cellular systems in each market (25 megahertz for each system). This policy of initially licensing two facilities-based sellers helped to create the competitive wireless industry we have today with numerous choices available to consumers (e.g., personal communications services or PCS[51]) in addition to cellular service. Throughout the period of

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Handbook of Experimental Economics, edited by John H. Kagel and Alvin E. Roth, Princeton University Press, 1995.

[48] "Board of Directors for 'New' Boeing Company Announced," Boeing New Release, http://www.boeing.com/news/releases/1997/news_release_970801a.html.

[49] Statement of Chairman Robert Pitofsky and Commissioners Janet D. Steiger, Roscoe B. Starek III and Christine A. Varney in the Matter of The Boeing Company/McDonnell Douglas Corporation, File No. 971-0051, http://www.ftc.gov/opa/1997/07/boeingsta.htm.

[50] Resellers of cellular service were allowed to exist in each area as well.

[51] Broadband PCS is similar to cellular service. One exception is that broadband PCS systems operate in different spectrum bands than cellular systems. Broadband PCS licenses have been assigned through auction since 1995.

competition between the two facilities based providers of cellular service, average local monthly bills for cellular service declined steadily from $98.02 in 1988 to $39.43 in 1998.[52]

D. Entry Conditions

For many pharmaceutical products, new competition emerges from R&D activities. Such R&D has already occurred and is ongoing with respect to albuterol. Competitive responses, which likely were stimulated by the proposed policy change with regard to CFC MDIs, resulted in pharmaceutical firms conducting R&D to develop new, improved delivery systems for albuterol. GSK spent nearly $1 billion developing CFC-free delivery systems. Other firms such as suppliers of the HFA gas and manufacturers of the components for the HFA inhalers also invested resources in preparing for the transition to a CFC-free world.

Establishing that additional sellers of albuterol in non-CFC MDIs are likely to emerge beyond the two already approved sellers is not relevant to the FDA decision on removing the essential-use designation for albuterol MDIs. However, entry into production and sale of albuterol products is possible. Albuterol is not patented. Anyone can market a product containing albuterol as the underlying chemical. The owner of a HFA technology (3M) continues to express interest in licensing the technology to additional licensees.[53] Other pharmaceutical firms already have knowledge and experience with methods for treating asthma and COPD as well as the FDA regulatory process to obtain product approvals of albuterol in non-CFC delivery systems in a timely manner.

"IVAX has invested many millions of dollars over the past seventeen years to bring CFC-free products to the U.S. and European markets."[54] IVAX submitted two NDAs for CFC-free formulations of albuterol to the FDA in 2003.[55] The first NDA is for a HFA formulation of albuterol in MDIs, and the second NDA is for a formulation of albuterol in its patented

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[52] Cellular Telecommunications & Internet Association, "Background on CTIA's Semi-Annual Wireless Industry Survey," http://files.ctia.org/pdf/CTIA_Semiannual_Survey_YE2003.pdf.

[53] "3M Seeking Partners for its Biotech Drug Delivery Technologies," 3M press release, June 10, 2002, http://www.3m.com/us/healthcare/manufacturers/dds/jhtml/press_releases.jhtml.

[54] See statement of Neil Flanzraich, PADAC Meeting Transcript, p. 154.

[55] "IVAX Submits New Drug Application for CFC-Free Albuterol," September 2, 2003. IVAX press release available at http://www.ivax.com.

breath activated Easi-Breathe® inhaler. IVAX received an approvable letter from the FDA for the first (albuterol HFA MDI) NDA in December 2003, and IVAX recently received an approvable letter from the FDA for the second (Easi-Breathe®) NDA in July 2004.[56] IVAX claims that, once approved for marketing, these products will compete with the existing albuterol HFA MDIs.[57]

Sepracor is also developing a competing product, levalbuterol HFA MDI, which is similar to albuterol HFA MDIs, to sell in the U.S.[58] Levalbuterol is a CFC-free, short acting, beta-agonist that is a purified form of albuterol. Sepracor submitted an NDA to the FDA in May 2004.[59] Sepracor has announced that it has been notified that "March 12, 2005...is the date by which the FDA is expected to review and act on an NDA submission" for the Xopenex HFA® MDI.[60]

After the policy change, there will be at least two competing sellers of brand albuterol HFA MDIs. The two existing sellers of albuterol HFA MDIs have competed vigorously in the past selling brand albuterol CFC MDIs. In addition, there are albuterol products under review at the FDA, new asthma or COPD drugs in development, and potential entrants able to combine the non-patented albuterol and a license for a new (non-CFC) delivery system. These conditions suggest that rivalry will exist in the marketplace after the policy change. The rivalry will benefit patients by providing more information on asthma and COPD, more choices for treating the diseases, and price competition.

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[56] "IVAX' Albuterol HFA Approvable by FDA," and "IVAX Receives FDA Approvable Letter for Albuterol HFA in Breath-Activated Inhaler," December 1, 2003 and July 7, 2004, respectively. IVAX press releases available at http://www.ivax.com.

[57] PADAC Meeting Transcript, pp. 158-60.

[58] Levalbuterol is currently available as a nebulizer solution. "Xonepex® (levalbuterol)," http://www.sepracor.com/therap/xopenex.html.

[59] "Sepracor Submits New Drug Application for XOPENEX HFA® Metered-Dose Inhaler to FDA," May 13, 2004, http://www.prnewswire.com/cgi-bin/stories.pl?ACCT=105&STORY=/www/story/05-13-2004/0002173499. See also the comment by William McVicker from Sepracor , PADAC Meeting Transcript, p. 216.

[60] "XOPENEX HFA® Metered-Dose Inhaler NDA Filed by FDA," July 15, 2004, http://www.pharmalive.com/NEWS/index.cfm?articleid=154194&categoryid=51.

V. ESTIMATES OF THE PRICE ELASTICITY OF DEMAND

The Notice express a concern that "higher prices [after the policy change] will discourage some patients from buying albuterol."[61] The estimate in the Notice is that the effect of the price increase could potentially reduce the use of albuterol by "400,000 to 1 million MDIs per year."[62] The conclusion elsewhere in the Notice is that "[t]he best evidence available to us indicates that the demand for prescription drugs is generally quite inelastic with respect to price changes, so even this relatively large price increase is likely to cause changes in the consumption of MDIs that are quite small relative to the market."[63]

The estimates of reduced use of albuterol MDIs are based on information in two recent articles by Goldman et al. and Ringel et al.[64] that address healthcare issues unrelated to the present matter. These sources do not study explicitly the marketplace for selling albuterol MDIs or the effect of price increases for any product on uninsured or low-income patients. Most notably, in contrast to the information from these studies, our albuterol-specific data suggest that, in the two years following entry by generic versions of albuterol CFC MDIs at presumably lower prices compared to brand products, there was a *drop* in total prescriptions for albuterol MDIs. That is, both the average price fell and the total usage fell. This result may reflect that there are better maintenance medications for asthma and COPD reducing the need for rescue medications and/or the reduction in advertising of the brand products around the time of entry by the generic versions of albuterol CFC MDIs. However, as pointed out in the Notice, albuterol MDI is a rescue medication, which is used in emergency situations.[65] Therefore, it is unlikely that a given patient would have the same sensitivity to price for albuterol MDIs as for other pharmaceutical products.

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[61] Notice, p. 33609.

[62] Notice, p. 33610.

[63] Notice, p. 33607.

[64] Dana P. Goldman, Geoffrey F. Joyce, Jose J. Escarce, Jennifer E. Pace, Matthew D. Solomon, Marianne Laouri, Pamela B. Landsman, and Steven M. Teutsch, "Pharmacy Benefits and the Use of Drugs by the Chronically Ill," *Journal of the American Medical Association*, Vol. 291, No. 19, May 19, 2004, pp. 2344-50; and Jeanne S. Ringel, Susan D. Hosek, Ben A. Vollaard, and Sergej Mahnovski, "The Elasticity of Demand for Health Care: A Review of the Literature and its Application to the Military Health System," National Defense Research Institute, Rand Health, 2002. See Notice, pp. 33610 and 33615.

[65] Notice, p. 33615.

The Goldman et al. study considers asthma products that include "anti-cholinergics, anti-inflammatory asthma agents, leukotreine modulators, oral steroids, steroid inhalers, sympathomimetics, and xanthines."[66] Within the sympathomimetic class for the population between 18 and 64 years old, the six most frequently prescribed products in 2000 were: albuterol CFC MDIs, guaifenesin/phenylpropanolamine, Serevent®, Combivent®, guaifenesin/pseudoephedrine hydrochloride, and albuterol sulfate.[67] Even within the sympathomimetic class, the products considered by Goldman et al. have different characteristics. There are products for which only a brand version is available (e.g., Serevent® and Combivent®), brand and generic versions are available (e.g., albuterol), over-the–counter versions are available (e.g., guaifenesin/phenylpropanolamine and guaifenesin/pseudoephedrine hydrochloride), rescue and maintenance products for asthma (e.g., albuterol and Serevent®), and the approved indications differ (e.g., asthma/COPD and cough/cold). Given these differences across the products that Goldman et al. consider as treatments for asthma, meaningful conclusions about the price elasticity of demand for a particular product in this group (e.g., albuterol) cannot be drawn from the study. In fact, demand for a cough/cold remedy such as guaifenesin/phenylpropanolamine, which is sold over-the-counter under at least 20 brand names,[68] will be more sensitive to a price change (i.e., elastic) than demand for albuterol MDIs. Maintenance products for asthma will likely have a greater sensitivity to changes in co-payments compared to rescue medications. In general, the individual products in the asthma category considered by Goldman et al. are likely to have different price elasticities of demand. Thus, it is incorrect to apply the results obtained from analyzing a group of differentiated products uniformly to each product in the group.[69]

The Goldman et al. article is not directly comparable to the situation analyzed in the Notice. Goldman et al. state that the "sample was drawn from an insured working-age

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[66] Dana P. Goldman, Geoffrey F. Joyce, Jose J. Escarce, Jennifer E. Pace, Matthew D. Solomon, Marianne Laouri, Pamela B. Landsman, and Steven M. Teutsch, "Pharmacy Benefits and the Use of Drugs by the Chronically Ill," *Journal of the American Medical Association*, Vol. 291, No. 19, May 19, 2004, p. 2346.

[67] Dana P. Goldman, Private Communication, July 29, 2004.

[68] See http://www.umm.edu/altmed/ConsDrugs/GuaifenesinandPhenylpropanolaminecd.html.

[69] Jerry Hausman, Gregory Leonard, and J. Douglas Zona, "Competitive Analysis with Differenciated Products," *Annales D'Economie et De Statistique*, Vol. 34, 1994, pp. 159-180.

population, and thus [their] results are not necessarily generalizable to other populations such as the poor or the elderly."[70] To compensate for the lack of direct comparability, the assumption in the Notice about the price elasticity of demand for albuterol MDIs is that demand is more inelastic than suggested by the results described by Goldman et al. The analysis in the Notice assumes arbitrarily that the elasticity is -0.05 without an explanation.[71] It is equally plausible that the elasticity is -0.01 as opposed to -0.05. Applying the formula in the Notice for estimating the reduction in albuterol MDIs purchased yields a lower bound of 72,000 MDIs, not 360,000 MDIs.

The Ringel et al. study is a survey of the economic literature on attempts to measure price elasticity of demand. The authors survey literature in which the products considered, the data used, the time periods covered, and the statistical methods applied differ across studies. In no case did any of the material surveyed by Ringel et al. measure the price elasticity of demand for albuterol MDIs. As expected given the diversity of the literature surveyed, the measures of price elasticity of demand discussed by Ringel et al. vary widely.

Relying on the Goldman et al. study of asthma products and the Ringel et al. survey of studies across a broad set of pharmaceuticals leads to erroneous conclusions. The demand for albuterol MDIs is likely to be more inelastic than the demand for pharmaceutical products studied by Goldman et al. and Ringel et al. The three relevant product characteristics that suggest demand for albuterol MDIs is inelastic are that:

- albuterol MDIs are a necessity for patients with asthma or COPD,
- they are the standard for rescue therapy in these patients, and
- they have a low price per prescription relative to the average price of a prescription for a brand product generally.

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[70] Dana P. Goldman, Geoffrey F. Joyce, Jose J. Escarce, Jennifer E. Pace, Matthew D. Solomon, Marianne Laouri, Pamela B. Landsman, and Steven M. Teutsch, "Pharmacy Benefits and the Use of Drugs by the Chronically Ill," *Journal of the American Medical Association*, Vol. 291, No. 19, May 19, 2004, p. 2349.

[71] Notice, p. 33615

These product characteristics must be taken into account when attempting to measure precisely the amount by which demand for albuterol MDIs may fall in response to a price increase.

VI. MITIGATING FACTORS

In general, cash paying patients with asthma or COPD are not likely to forego consumption of a rescue medication. Nevertheless, product samples will be available to all patients. If a cash paying patient lacks the financial resources to purchase albuterol MDIs after the policy change, then the patient has options such as obtaining samples, relying on public and private patient assistance or discount programs, and accepting the Medicare prescription pharmaceutical benefit when available.

Patricia Danzon, a health economist from the University of Pennsylvania, recently considered a policy issue in the context of Medicare for which the price elasticity of demand is low and a proposed policy change might create an access barrier for a small group of patients. Her conclusion was not to abandon the policy, but rather focus directly on assisting those patients facing the access barrier. "If access barriers persist for low-income seniors, increasing the income-related subsidies would be a more target-efficient and economically efficient solution than increasing subsidies for everyone."[72] The implication of Danzon's work for the present matter is that rather than delay the policy change with regard to albuterol MDIs, the FDA should proceed with the rulemaking as long as there are sufficient programs targeted at those low income patients who may have difficulty paying for albuterol HFA MDIs. GSK's plans for distributing samples, freezing prices, offering coupons for Ventolin® HFA as well as the existing public and private patient assistance and discount programs are the appropriate targeted programs to alleviate the concerns about low income patients not having access to albuterol HFA MDIs. In the longer run, these programs together with new, improved products for asthma or COPD, buyer power, and prescription pharmaceutical coverage for Medicare enrollees in 2006 will help to maintain patient access to necessary medications.

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[72] Patricia M. Danzon, "Closing the Doughnut Hole: No Easy Answers," *Health Affairs*, Web Exclusive, July 21, 2004, p. W4-408.

A. Sampling

GSK has committed to provide 2 million samples of Ventolin® HFA MDIs per year through its sales representatives to physicians. These samples will be available free of charge to patients. Even if the estimates in the Notice that 400,000 to 1 million fewer albuterol MDIs will be purchased annually due to the higher prices resulting from the policy change were accurate, GSK alone is making available two times the upper bound number of Ventolin® HFA MDIs at no cost to patients. These samples will provide all patients with access to albuterol HFA MDIs. Since physicians routinely distribute samples to help the low-income or uninsured patients, these patents will be major beneficiaries of these samples. Consider the following views we identified from the literature.

- "Doctors used the samples to test for efficacy and tolerance, provide temporary relief or convenience to the patient, or to save medication costs for poorer patients."[73]
- "The bulk of promotional spending is for sampling, or giving free drug samples directly to physicians. Physicians may distribute these free samples to patients, who otherwise would need to order the drugs from a pharmacy and typically would pay some out-of-pocket cost to fill prescriptions."[74]
- "Drug samples were the most common resource that clinic sites used to treat low-income asthma patients."[75]

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[73] Agency for Healthcare Research and Quality, "Medical Practices Can Benefit from Specific Policies for Interacting with Pharmaceutical Representatives," *Research Activities*, No. 244, December 2000, http://www.ahrq.gov/research/dec00/1200RA9.htm#head2.

[74] Centers for Medicare & Medicaid Services, "Health Care Industry Market Update, Pharmaceuticals," January 10, 2003, p. 29, http://www.cms.hhs.gov/reports/hcimu/hcimu_01102003.pdf.

[75] Agency for Healthcare Research and Quality, "Health Care Costs and Financing, Community Health Centers Need More Resources to Provide Proper Care to High-Risk Asthma Patients," *Research Activities*, No. 231, November 1999, http://www.ahrq.gov/research/nov99/1199ra9.htm.

B. Patient Assistance, Discounts, and Medicare Rx Coverage

In addition to samples, public and private patient assistance or discount programs exist. By 2006, Medicare will provide enrollees with insurance coverage for prescription pharmaceuticals.

- PhRMA's patient assistance program website, HelpingPatients.org, provides information on over 285 patient assistance programs. Of these programs, about 35 percent are industry sponsored, and about 65 percent are government or privately sponsored.[76]
- Both Schering and GSK have patient assistance programs that apply to Proventil® HFA and Ventolin® HFA.[77] After the policy change, GSK will distribute more information about its *Bridges to Access* program and its other initiatives to patients and healthcare providers.
- We understand that GSK will make available 3 million *Ventolin HFA Savings Checks* at $10 each.[78] These coupons will be available to all patients (cash or insured) throughout the U.S. to use immediately upon purchase of the product at the pharmacy.[79] They will be in addition to the existing discount programs that GSK offers: *GSK Orange Card* and *Together Rx*.[80]
- Medicare will offer an outpatient prescription pharmaceutical insurance plan to enrollees in 2006. According to the Centers for Medicare & Medicare Services ("CMS"), approximately 4.5 million Medicare beneficiaries eligible for low-income assistance will enroll in this benefit during the first year.[81] According to

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[76] Interview with Preet Bajua, PhRMA. Examples of public patient assistance programs that provide albuterol MDIs are DC Healthcare Alliance and DC Healthy Families.

[77] PADAC Meeting Transcript, pp. 136-8.

[78] A patient's cost will have to be $10 or more per prescription before the coupon will apply to the transaction. For example, a patient with a co-payment of only $5 per prescription will not be eligible to use to coupon.

[79] GSK Comments, Section 2.2.1.1.3.

[80] We discussed these programs in our previous submission (pp. 20-1)

[81] CMS estimates that 14.5 million beneficiaries will be eligible for low-income subsidies in 2006. Of these beneficiaries, 6.4 million are currently covered under Medicaid and will automatically be enrolled in the Medicare prescription pharmaceutical plan. According to CMS, approximately 56 percent of the remaining 8.1

the National Health Interview Survey, 5.7 percent of people enrolled in Medicare were diagnosed with asthma in 2002.[82] Using these estimates, approximately 258,552 of the low-income Medicare enrollees will be diagnosed with asthma in 2006. From our previous estimates that 50 million albuterol MDIs are sold annually and 20.3 million people in the U.S. are diagnosed with asthma,[83] there are approximately 2.5 albuterol MDIs prescribed for every person diagnosed with asthma. Thus, the number of albuterol MDIs that will be provided to low-income Medicare enrollees with asthma through the prescription pharmaceutical plan in 2006 is 646,380 MDIs (258,552 x 2.5).

C. Price Freeze

As pointed out in the Notice,[84] GSK has announced a voluntary price freeze for Ventolin® HFA. Prices for all payers should remain stable. However, GSK cannot control prices for its products charged by other participants in the pharmaceutical industry (e.g., wholesalers and retailers).

D. Analyses with Mitigating Factors

1. NERA Model

We incorporated several of the factors that alleviate directly any concerns about patients not having access to albuterol MDIs after the policy change into the original model from our previous submission. Specifically, we introduced explicitly into our model the effects of product samples, patient assistance programs, and coupons on the average price of albuterol

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million beneficiaries will enroll in the Medicare prescription pharmaceutical plan. "CMS Predicts 11 Mil. Low-Income Seniors Will Enroll In Medicare Rx," *The Pink Sheet*, August 2, 2004, p. 28.

[82] U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics, "Summary Health Statistics for U.S. Adults: National Health Interview Survey, 2002," Vital Health Statistics, Series 10, Number 222, July 2004, pp. 22-3, http://www.cdc.gov/nchs/data/series/sr_10/sr10_222acc.pdf.

[83] See Exhibit 6 in our previous submission.

[84] Notice, p. 33616.

MDIs after the policy change. The effects of these changes compared to our original model are as follows.

- Two million samples of Ventolin® HFA will be available to patients at zero price. Our new results are:
  - the total first year impact of the policy change is reduced from $494 million to $437 million, and
  - the total change in costs per MDI is reduced from $9.87 ($7.33 and $2.54 for patients and third-party payers, respectively) to $8.74 ($6.63 and $2.11 for patients and third-party payers, respectively).
- In addition to the two million samples of Ventolin® HFA from GSK, we assume 1 million albuterol MDIs programs will be available to low-income patients from Schering's samples and public and private patient assistance programs. Our new results are:
  - the total first year impact of the policy change is reduced to $409 million, and
  - the total change in costs per MDI is reduced to $8.18 ($6.28 and $1.90 to patients and third-party payers, respectively).
- In addition to the 3 million albuterol MDIs available through samples and patient assistance programs, we assume that patients redeem 1 million (or 33.3 percent)[85] of the $10 *Ventolin HFA Savings Checks*. Our new results are:
  - the total first year impact of the policy change is reduced to $399 million, and
  - the total change in costs per MDI is reduced to $7.98.

The impact of just these three factors alone reduces the cost to the healthcare system in the first year by over 19 percent from our worst-case estimate.

[85] If redemption rate for the coupons is greater than 33.3 percent, then the financial impact of the policy change will be further reduced.

2. Notice

We also considered the effects of certain marketplace characteristics on the estimates presented in the Notice regarding the potential number of albuterol MDIs not purchased after the policy change. The lower and upper bounds used in the Notice on the number of albuterol MDIs not purchased are 400,000 and 1 million.[86] Based on our review of the information in the Notice on elasticity discussed above, we concluded that even these estimates are too high. However, we use the range in the Notice merely for illustration. First, GSK intends to distribute 2 million samples of Ventolin® HFA. If these samples are distributed to uninsured patients in proportion to their presence in the general population (15 percent as in the Notice),[87] there will be 300,000 samples of Ventolin® HFA given free to low-income patients. The samples reduce the number of MDIs at issue in the Notice by 300,000 MDIs. The patients receiving samples will be better off than they are today when they pay for albuterol MDIs. Since samples are more likely to be given by physicians to low-income patients, the estimate of 300,000 understates the impact of the samples on addressing the estimates in the Notice.

Public and private patient assistance programs provide another source of free albuterol MDIs for patients. For example, GSK alone distributed 66,213 and 79,861 Ventolin® MDIs in 2003 and 2004 (January-July),[88] respectively. GSK accounted for relatively small shares of the total albuterol MDIs sold during these years. Since GSK's presence in the marketplace for selling albuterol MDIs will increase after the policy change, it will likely receive more requests for albuterol MDIs through its *Bridges to Access* program as well as its discount programs: *GSK Orange Card* and *Together Rx*. At a minimum, GSK will likely continue receiving requests for Ventolin® HFA at the same rate as in 2004.

Finally, the Medicare prescription pharmaceutical plan will provide benefits to patients in 2006. We estimate that the plan will provide approximately 646,380 MDIs per year to low-income patients with asthma.

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[86] Notice pp. 33615-6. The actual range is 360,000 to 1,080,000.

[87] Notice p. 33615.

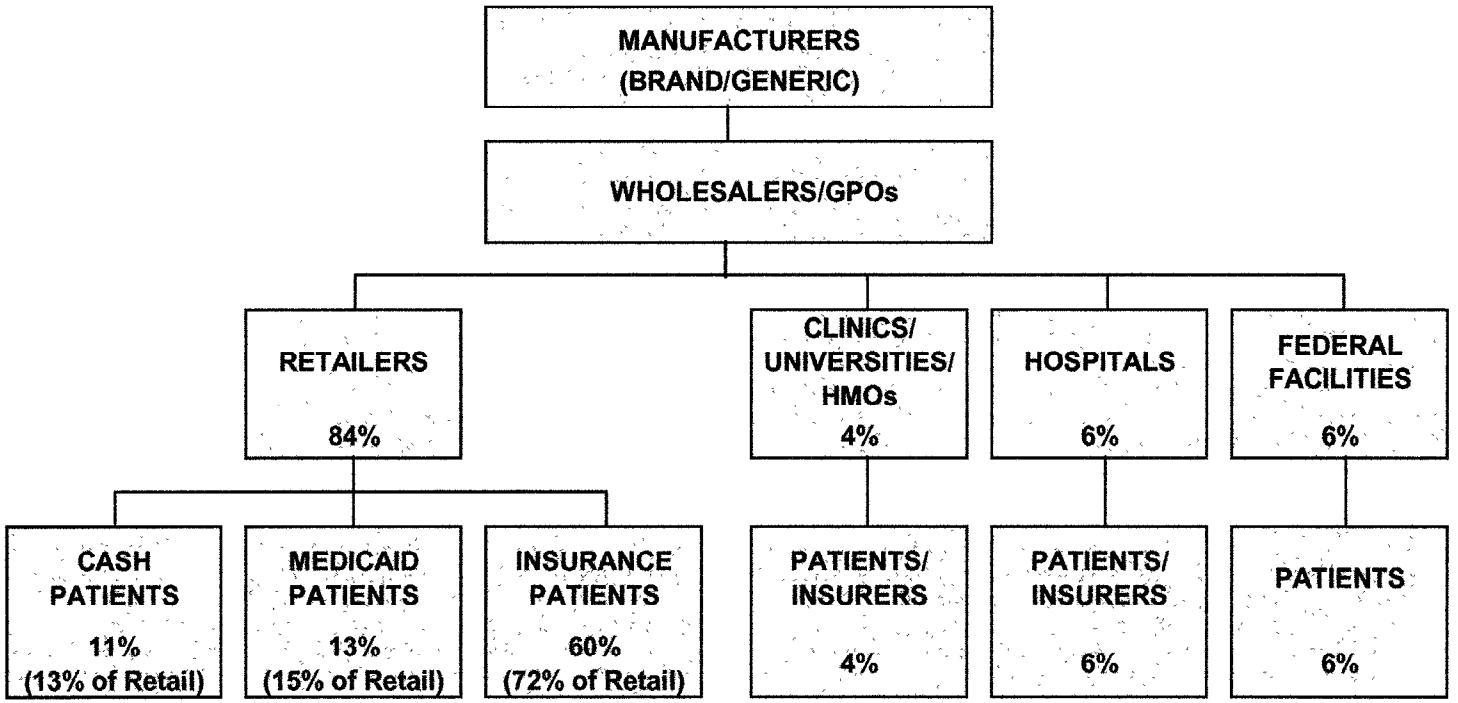
[88] Based on seven months of data, the number of Ventolin® HFA MDIs GSK can expect to distribute in 2004 is 136,905. See GSK Comments, Section 2.2.4.1.4.

GSK's samples and *Bridges to Access* program plus the Medicare prescription pharmaceutical plan will likely provide more than 1 million albuterol MDIs annually to low-income patients. See Exhibit 11. The number of albuterol MDIs available through these three programs exceeds the upper bound of the range used in the Notice. Thus, low-income patients will be adequately served.

VIII. CONCLUSION

We conclude that the economic evidence supports a near-term effective date for removing the essential-use designation for albuterol MDIs. All patients will continue to be adequately served after the policy change. In that regard, the FDA should adopt December 31, 2005 as the effective date for the policy change. We found no economic factors to support any other date.

VERTICAL STRUCTURE OF THE PHARMACEUTICAL SECTOR AND THE DISTRIBUTION OF ALBUTEROL MDIs

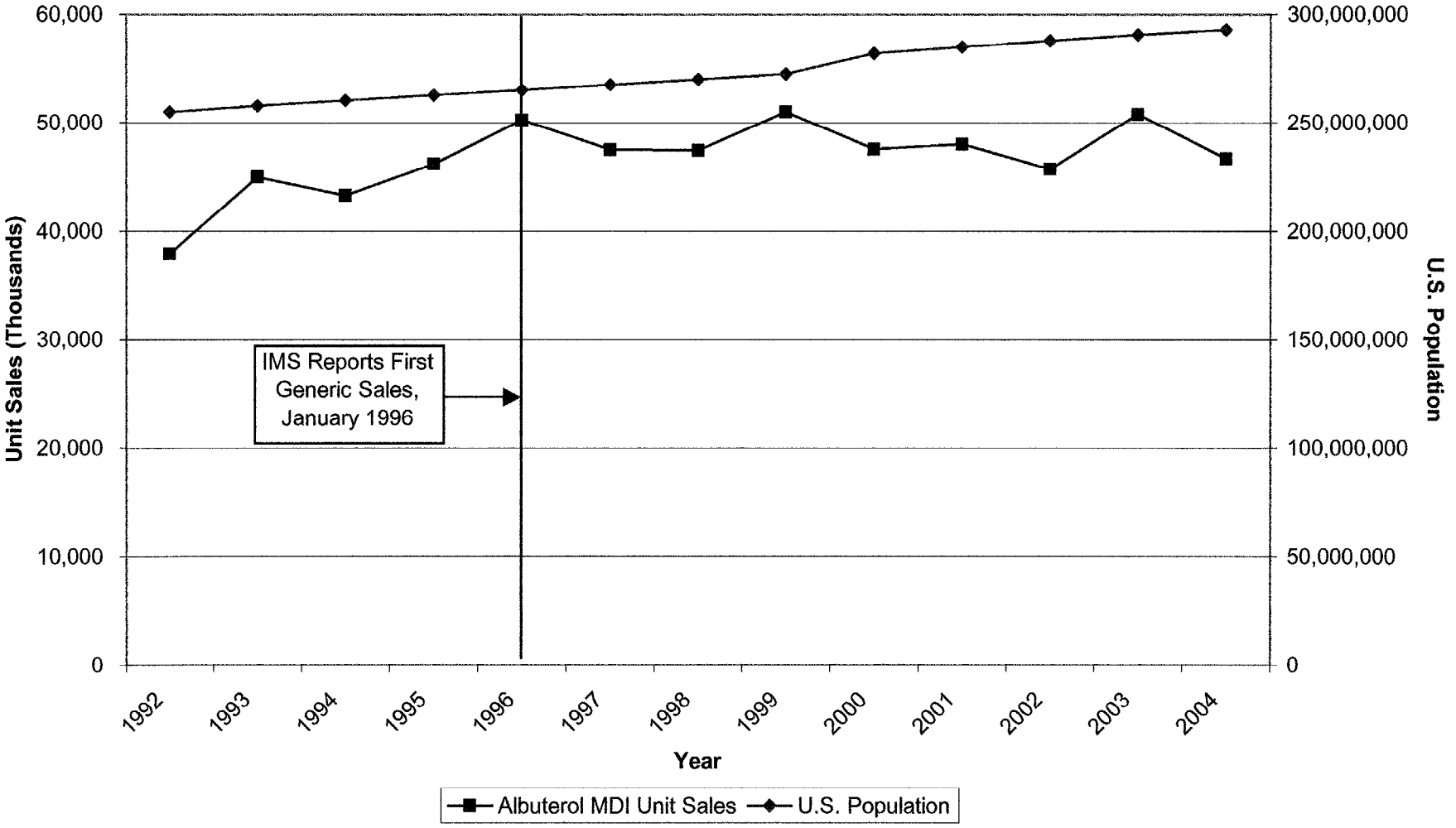


Source: IMS data; and Verispan data.

Exhibit 2

TOTAL ALBUTEROL MDI UNIT SALES AND U.S. POPULATION

1992 - 2004



Note: Albuterol MDI Unit Sales data in 1992 to 1997 adjusted for mail order and annualized in 2004.

Source: IMS data; and U.S. Census Bureau.

ANNUAL CHANGE IN TOTAL ALBUTEROL MDI UNIT SALES

Year	Total albuterol MDI Unit Sales (Units) (1)	Annual Change in Total albuterol MDI Unit Sales (Units) (2)
1992	37,915,000	-
1993	44,930,000	7,015,000
1994	43,257,000	(1,673,000)
1995	46,164,000	2,907,000
1996	50,242,000	4,078,000
1997	47,525,000	(2,717,000)
1998	47,437,000	(88,000)
1999	51,003,000	3,566,000
2000	47,547,000	(3,456,000)
2001	47,999,000	452,000
2002	45,721,000	(2,278,000)
2003	50,779,000	5,058,000
2004	46,681,000	(4,098,000)

( ) negative
- not applicable

Note: Data in 1992 to 1997 adjusted for mail order.
Data in 2004 annualized.

Source: IMS data.

Exhibit 4

SHARES OF ALBUTEROL MDI UNIT SALES BY SELLER

January 2004 - May 2004

Seller	Shares of albuterol MDIs (1) (Percent)
Schering-Plough Corporation[1]	64.1 %
IVAX Pharmaceutical	27.9
Andrx	6.7
GSK	0.7
Armstrong	0.6
Dey Labs Inc.	0.0
Pliva	0.0
Major Pharm	0.0
Total:	100 %

[1] Includes Warrick Pharmaceutical Corporation and Key Pharmaceuticals.

Source: IMS data.

LIST OF PRODUCTS WITH APPROVED INDICATION FOR ASTHMA OR COPD

BASED ON 2004 *PHYSICIANS' DESK REFERENCE*

Product (1)	Manufacturer (2)	Indication(s) (3)
1. Accolate Tablets	AstraZeneca	Bronchial Asthma
2. AccuNeb Inhalation Solution	Dey	Bronchial Asthma; Reversible Bronchospasm
3. Advair Diskus (3 strengths)	GSK	Bronchial Asthma
4. Aerobid Inhaler System	Forest	Bronchial Asthma
5. Aerobid-M Inhaler System	Forest	Bronchial Asthma
6. Alupent Inhalation Aerosol	Boehringer Ingelheim	Bronchial Asthma; Bronchospasm Associated with COPD; Reversible Bronchospasm
7. Atrovent Inhalation Aerosol	Boehringer Ingelheim	Bronchial Asthma; Bronchospasm Associated with COPD; Reversible Bronchospasm
8. Atrovent Inhalation Solution	Boehringer Ingelheim	Bronchospasm Associated with COPD; Reversible Bronchospasm
9. Azmacort Inhalation Aerosol	Aventis	Bronchial Asthma
10. Combivent Inhalation Aerosol	Boehringer Ingelheim	Bronchial Asthma
11. Decadron Tablets	Merck	Bronchial Asthma
12. Decadon Phosphate Injection	Merck	Bronchial Asthma
13. Depo-Medrol Injectable Suspension	Pfizer/Pharmacia & Upjohn	Bronchial Asthma
14. Depo-Medrol Single-Dose Vial	Pfizer/Pharmacia & Upjohn	Bronchial Asthma
15. DuoNeb Inhalation Solution	Dey	Bronchial Asthma
16. Flovent Inhalation Aerosol (3 strengths)	GSK	Bronchial Asthma
17 Flovent Rotadisk (3 strengths)	GSK	Bronchial Asthma
18. Hydrocortone Tablets	Merck	Bronchial Asthma
19. Hydrocortone Phosphate Injection	Merck	Bronchial Asthma
20. Intal Inhaler	Monarch	Bronchial Asthma
21. Maxair Autohaler	3M	Bronchial Asthma; Bronchospasm Associated with COPD
22. Orapred Oral Solution	Ascent	Bronchial Asthma
23. Pediapred Oral Solution	Celltech	Bronchial Asthma
24. Primatene Mist	Wyeth	Bronchial Asthma
25. Primatene Tablets	Wyeth	Bronchial Asthma
26. Pulmicort Respules	AstraZeneca	Bronchial Asthma
27. Pulmicort Turbuhaler Inhalation Powder	AstraZeneca	Bronchial Asthma
28. Qvar Inhalation Aerosol	IVAX	Bronchial Asthma
29. Serevent Diskus	GSK	Bronchial Asthma; Bronchospasm Associated with COPD; Exercise-Induced Bronchospasm; Prevention and Relief of Bronchospasm
30. Serevent Inhalation Aerosol	GSK	Bronchial Asthma; Bronchospasm Associated with COPD; Exercise-Induced Bronchospasm; Reversible Bronchospasm
31. Singular Oral Granules	Merck	Bronchial Asthma
32. Singular Tablets	Merck	Bronchial Asthma
33. Singular Chewable Tablets	Merck	Bronchial Asthma
34. Solu-Medrol Sterile Powder	Pfizer/Pharmacia & Upjohn	Bronchial Asthma
35. Tilade Inhaler	Monarch	Bronchial Asthma
36. Uniphyl Tablets (2 Strengths)	Purdue Frederick	Bronchial Asthma; Bronchospasm Associated with COPD; Reversible Bronchospasm
37. **Ventolin HFA Inhalation Aerosol**	**GSK**	Bronchial Asthma; Reversible Bronchospasm

LIST OF PRODUCTS WITH APPROVED INDICATION FOR ASTHMA OR COPD

BASED ON 2004 *PHYSICIANS' DESK REFERENCE*

Product (1)	Manufacturer (2)	Indication(s) (3)
38. VoSpire Extended-Release Tablets	Odyssey	Reversible Bronchospasm
39. Xolair	Genentech	Allergen Induced Asthma
40. Xopenex Inhalation Solution	Sepracor	Bronchial Asthma; Prevention and Relief of Bronchospasm; Reversible Bronchospasm

Note: Proventil HFA is not included in the 2004 *PDR.*
Represents 18 manufacturers.

Source: 2004 *Physicians' Desk Reference* .

LIST OF PRODUCTS IN DEVELOPMENT FOR ASTHMA OR COPD

Product (1)	Manufacturer (2)	Indication(s) (3)	Stage of Development (4)
1. 159797 (TD-3327) (beta2 agonist)	GSK	Asthma; COPD	Phase I
2. 597901 (beta2 agonist)	GSK	Asthma; COPD	Phase I
3. 799943 (glucocorticoid agonist)	GSK	Asthma	Phase I
4. albuterol sulfate (metered-dose solution inhaler)	Zambon	Asthma	Phase I
5. cromolyn	DURECT	Asthma	Phase I
6. IL-4/13 trap	Regeneron Pharmaceuticals	Asthma	Phase I
7. IPL 576,092	Aventis Pharmaceuticals	Asthma	Phase I
8. PDE 4 inhibitor	Schering-Plough	Asthma; COPD	Phase I
9. R1295 (integrin antagonist)	Roche	Asthma	Phase I
10. rhCC10	Claragen	Asthma; Pneumonia; End-Stage Renal Disease	Phase I
11. 681323 (p38 alpha kinase inhibitor)	GSK	Atherosclerosis; COPD	Phase I
12. IC485	ICOS	COPD	Phase I
13. anti-inflamatory compound	Aventis Pharmaceuticals	Asthma	Phase I/II
14. CpG 7909	Aventis Pharmaceuticals	Allergies; Asthma; Breast Cancer; Melanoma Cancer; Renal Cancer; Hepatitis B; Non-Hodgkin's Lymphoma	Phase I/II
15. Solomagen	Genaera	Asthma; COPD	Phase I/II
16. 274150 (selective iNOS inhibitor, oral)	GSK	Asthma; COPD; Migraine	Phase II
17. 559090 (alpha4 integrin antagonist)	GSK	Asthma	Phase II
18. 685698 (glucocorticoid agonist)	GSK	Asthma	Phase II
19. 766994 (chemokine receptor 3 antagonist, oral)	GSK	Asthma	Phase II
20. 842470 (PDE IV inhibitor)	GSK	Asthma; COPD	Phase II
21. bimosiamose	Encysive Pharmaceuticals	Asthma	Phase II
22. daclizumab (anti-CD25)	Protein Design Labs	Asthma	Phase II
23. EPI-2010	EpiGenesis Pharmaceuticals	Asthma; COPD	Phase II
24. IPL-512602	Inflazyme Pharmaceuticals	Asthma	Phase II
25. lidocane solution for inhalation	Corus Pharma	Asthma	Phase II
26. mepolizumab (anti-IL-5 MAb)	GSK	Asthma	Phase II
27. NGD-2001	Neurogen	Asthma; Rheumatoid Arthritis	Phase II
28. R411	Roche	Asthma	Phase II
29. formoterol HFA	SkyePharma	Asthma	Phase II completed
30. QVAR	IVAX	Asthma	Phase II completed
31. ML-03	Milkhaus Laboratory	Bronchitis; COPD; Cystic Fibrosis	Phase II completed
32. Aerobid	Forest Laboratories	Asthma	Phase III
33. Allegra	Aventis Pharmaceuticals	Asthma	Phase III
34. roflumilast	Altana Pharma	Asthma; COPD	Phase III
35. Symbicort pMDI	AstraZeneca	Asthma	Phase III
36. Xolair	Genentech	Asthma	Phase III

LIST OF PRODUCTS IN DEVELOPMENT FOR ASTHMA OR COPD

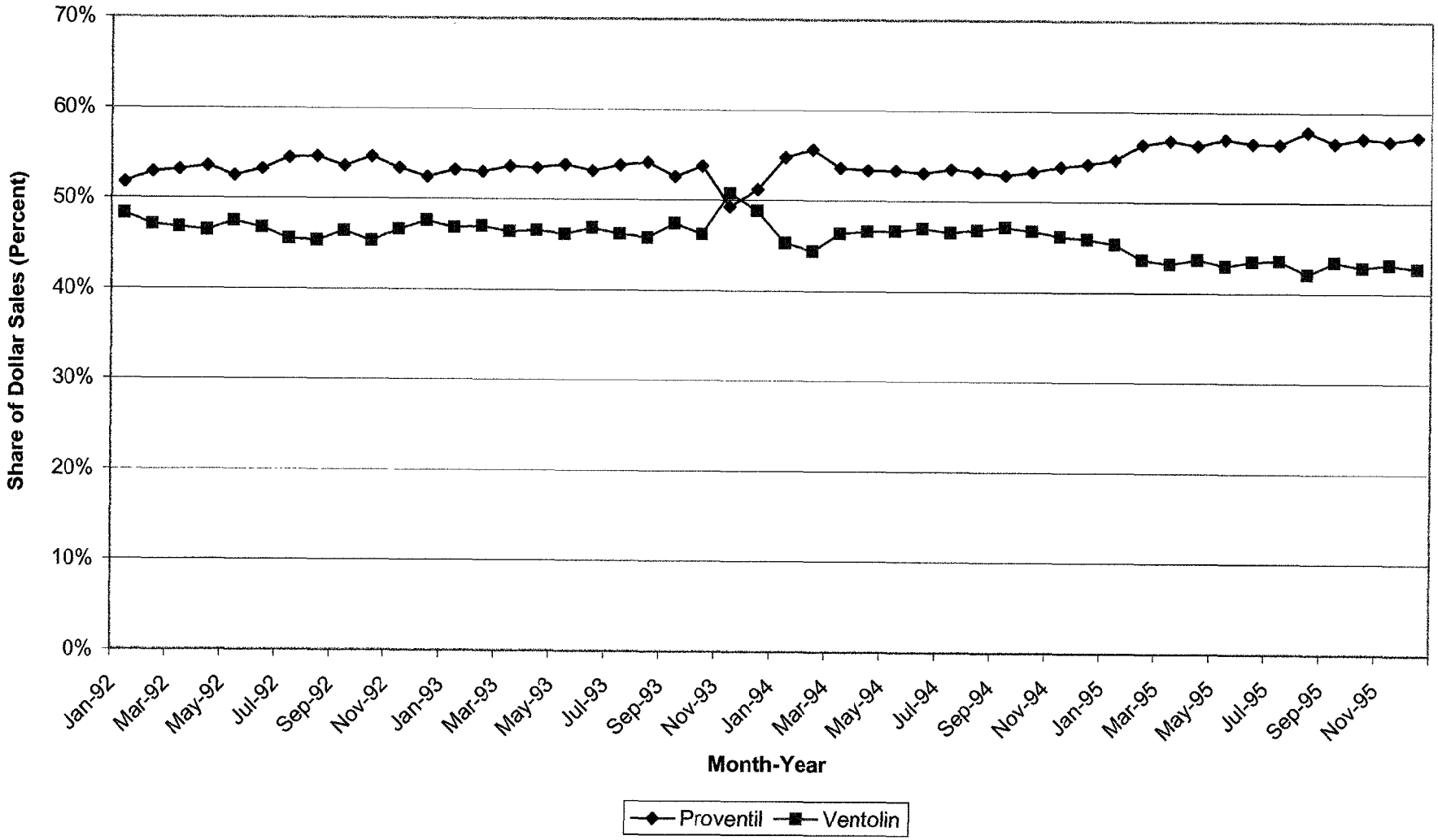
Product (1)	Manufacturer (2)	Indication(s) (3)	Stage of Development (4)
37. Advair	GSK	COPD	Phase III
38. arformoterol	Sepracor	COPD	Phase III
39. Singulair	Merck	Asthma	Phase IV
40. R 113281 (tachykinin receptor antagonist)	Sankyo Pharma	Asthma; COPD	In clinical trials
41. Volare	IVAX	Asthma; Bronchospasm	Application submitted/Phase III
42. Aerospan	Forest Laboratories	Asthma	Application submitted
43. Alvesco	Aventis Pharmaceuticals	Asthma	Application submitted
44. Xopenex HFA MDI	Sepracor	Asthma; COPD	Application submitted
45. Formadil Aerolizer	Novartis Pharmaceuticals	COPD	Application submitted
46. Spiriva	Boehringer-Ingelheim Pharmaceuticals	COPD	Application submitted
47. pramorelin	Wyeth Pharmaceuticals	Asthma	na

na not available

Source: PhRMA, "New Medicines in Development" for Asthma and COPD, extracted August 6, 2004.

SHARE OF DOLLAR SALES FOR PROVENTIL CFC AND VENTOLIN CFC

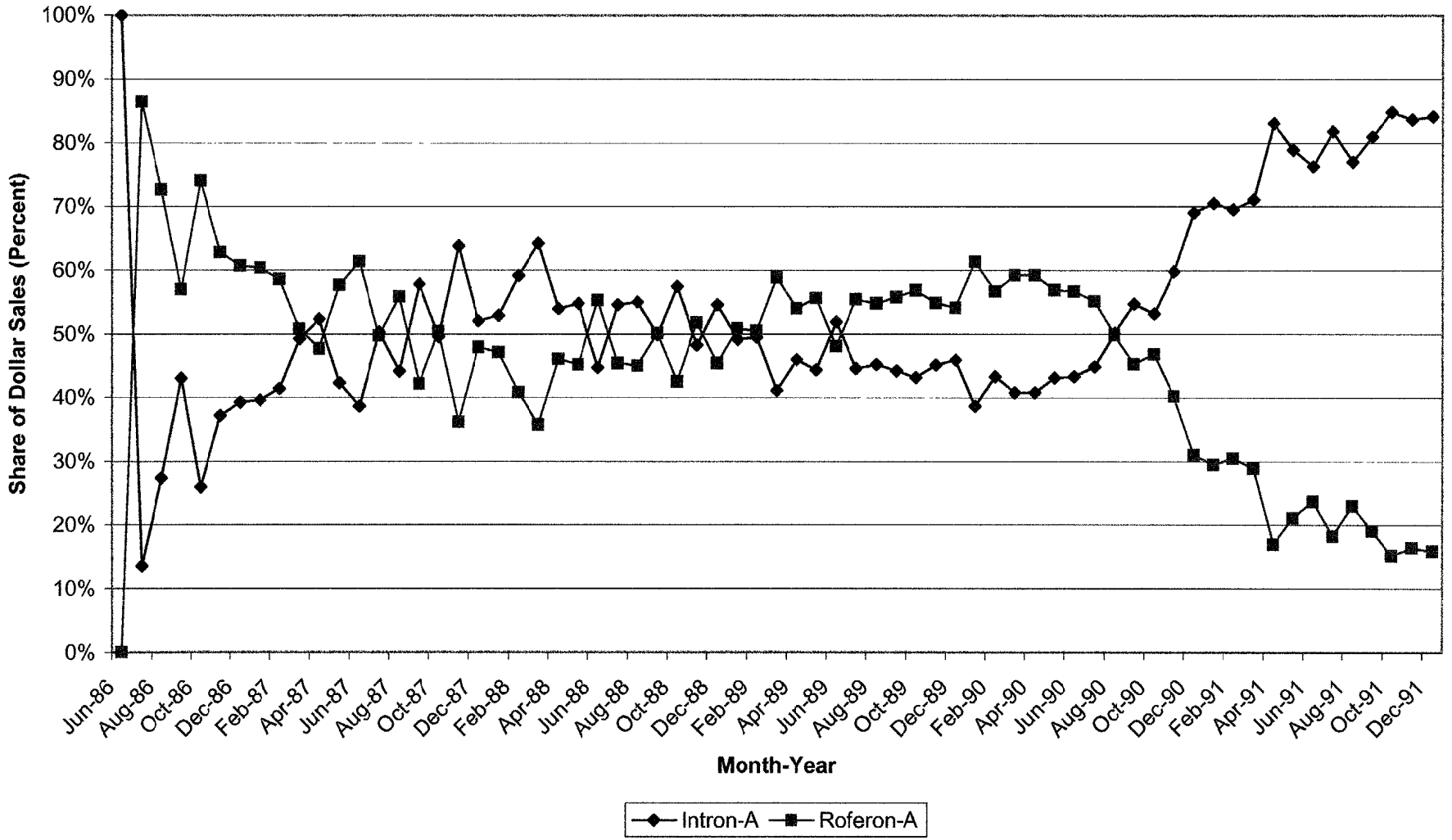
January 1992 - December 1995



Source: IMS data.

SHARE OF DOLLAR SALES FOR INTRON-A AND ROFERON-A

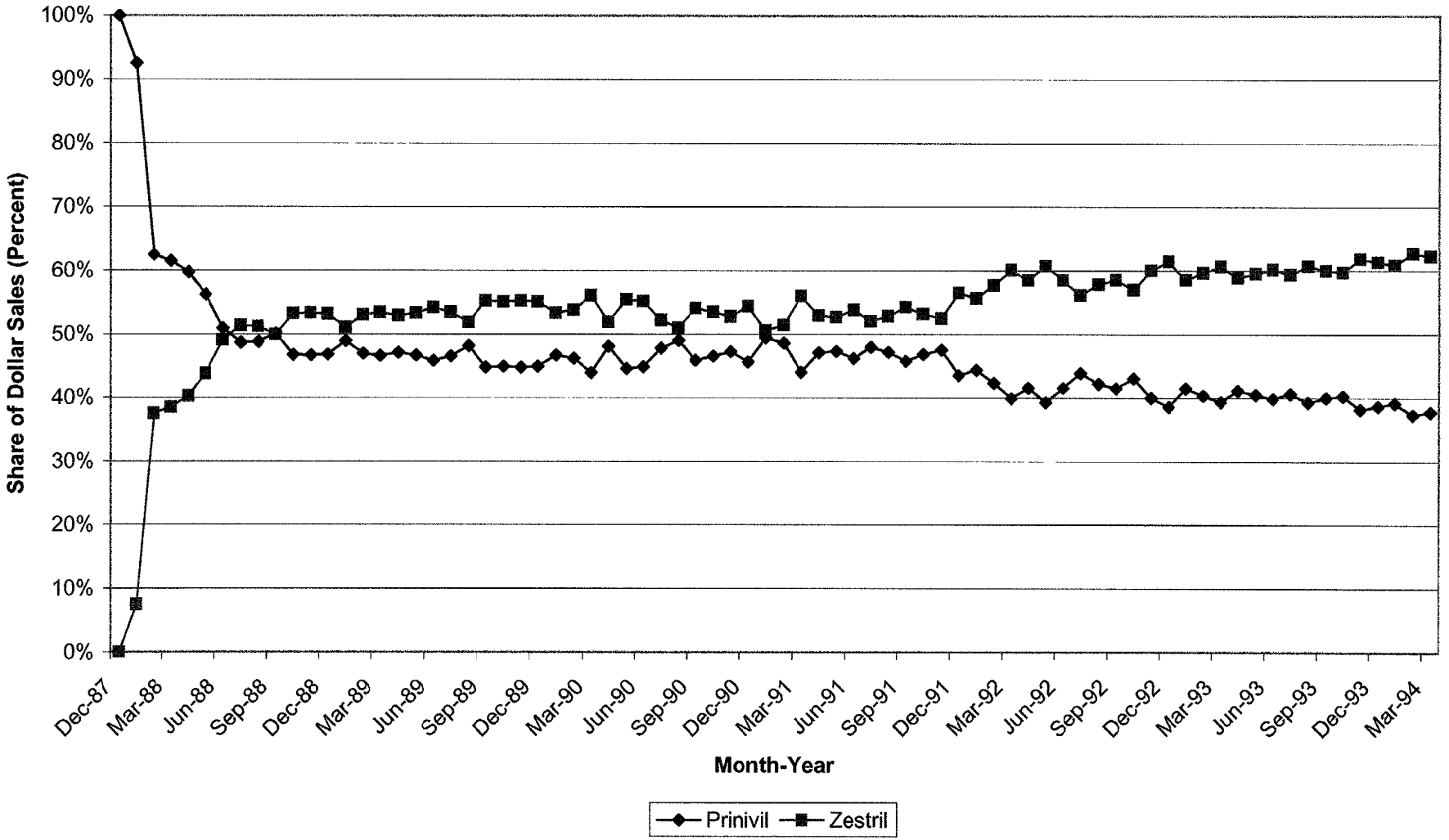
June 1986 - December 1991



Source: IMS data.

SHARE OF DOLLAR SALES FOR PRINIVIL AND ZESTRIL

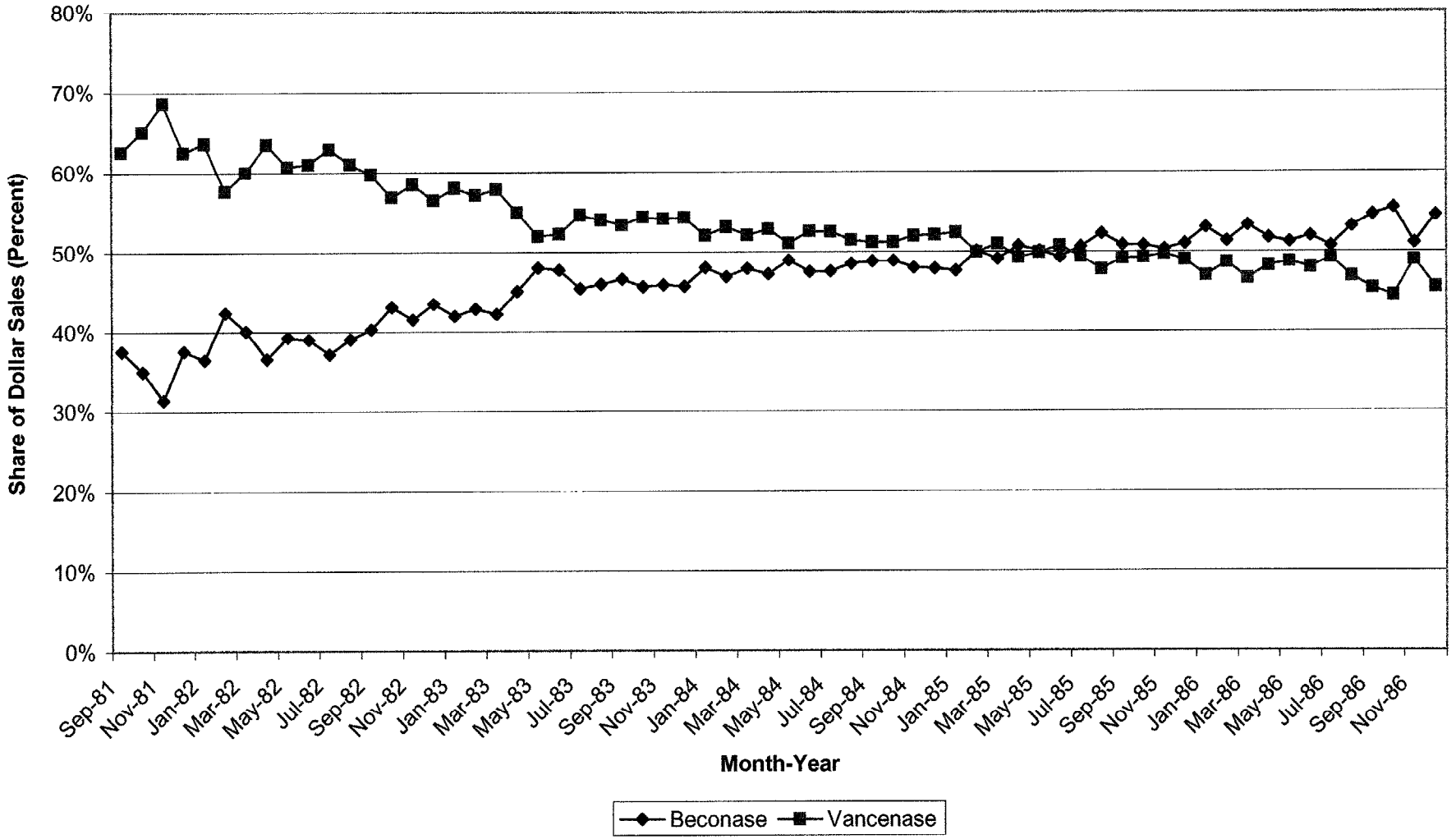
December 1987 - March 1994



Source: IMS data.

SHARE OF DOLLAR SALES FOR BECONASE AND VANCENASE

September 1981 - December 1986



Source: IMS data.

SELECTED PROGRAMS MORE THAN COMPENSATE FOR ANY REDUCTION IN DEMAND FOR ALBUTEROL MDIs DUE TO HIGHER PRICES

	Lower Bound (1)		Upper Bound (2)	
Calculation in Notice (A through F):				
A. Number of Generic albuterol MDIs Sold Annually[1]	40,000,000	MDIs	40,000,000	MDIs
B. Percent of Population without Insurance[1]	15	%	15	%
C. Number of Generic albuterol MDIs Sold Annually to Uninsured Patients (AxB)	6,000,000	MDIs	6,000,000	MDIs
D. Price Elasticity of Demand Estimate[1]	0.05		0.10	
E. Brand to Generic Price Ratio[1]	1.20		1.80	
F. Notice Estimate of Reduction in Annual Demand for albuterol MDIs[1] (CxDxE)	**360,000**	**MDIs**	**1,080,000**	**MDIs**

Selected Programs (G through O):		
G. GSK Commitment to Provide Annual Samples of Ventolin HFA MDIs[2]	2,000,000	MDIs
H. GSK Samples Provided to Uninsured Population Annually[3] (Gx15% or GxB)	300,000	MDIs
I. Annual Ventolin HFA MDIs provided through GSK Patient Assistance Program: Bridges to Access[4]	136,905	MDIs
J. Number of Medicare Beneficiaries Eligible for Low-Income Assistance Expected to Enroll in the Outpatient Prescription Drug Benefit Plan[5]	4,536,000	People
K. Percent of Medicare Enrollees Currently Diagnosed with Asthma[6]	5.7	%
L. Average Number of Medicare Enrollees Eligible for Low-Income Assistance Currently Diagnosed with Asthma (JxK)	258,552	People
M. Number of albuterol MDIs per Person Diagnosed with Asthma[7]	2.5	MDIs
N. Number of albuterol MDIs Provided under Medicare Prescription Drug Benefit Plan Annually (LxM)	646,380	MDIs
O. Total albuterol MDIs Provided Annually through Selected Programs[8] (H+I+N)	**1,083,285**	**MDIs**

SELECTED PROGRAMS MORE THAN COMPENSATE FOR ANY REDUCTION IN DEMAND FOR ALBUTEROL MDIs DUE TO HIGHER PRICES

[1] Notice, p. 33615.
[2] Notice, p. 33610.
[3] Assumes samples are distributed uniformly through population, rather than targeted to uninsured patients.
[4] Based on 79,861 Ventolin HFA MDIs provided by GSK from January to July, 2004.
[5] Represents estimated enrollment by the Centers for Medicare & Medicaid Services for the first year of the new outpatient prescription drug benefit. Excludes dual eligibles that are currently covered under Medicaid.
[6] Represents the percent of the Medicare population diagnosed with asthma that still have asthma.
[7] Based on an average of 50,000,000 MDIs sold annually and 20,300,000 people in the U.S. diagnosed with asthma in 2001.
[8] Represents GSK sampling program, GSK patient assistance program, and Medicare prescription drug plan only. Excludes Schering sampling, Schering patient assistance program, and other public and private patient assistance and discount programs.

Source: Notice, pp. 33610 and 33615; National Health Interview Survey, 2001 and 2002; "CMS Predicts 11 Mil. Low-Income Seniors Will Enroll In Medicare Rx," *The Pink Sheet*, August 2, 2004; and information provided by GSK.

APPENDIX
to
THE IMPACT ON PATIENTS AND PAYERS OF DESIGNATING ALBUTEROL A NON-ESSENTIAL USE OF AN OZONE DEPLETING SUBSTANCE

by
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Prepared in Response to Citizen Petition of the U.S. Stakeholders Group on MDI Transition (FDA Docket No. 03D-0029)

September 8, 2003

ESTIMATED ANNUAL WHOLESALERS' AND MANUFACTURERS' REVENUES FOR SALES OF BRAND AND GENERIC ALBUTEROL MDIs TO CASH, MEDICAID, AND INSURANCE PAYERS THROUGH GROUP 1 CHANNELS[1]

		Cash Payers (1)	Medicaid Payers (2)	Insurance Payers (3)
A.	Group 1, Total Unit Sales, 2001 - 2002	78,616,000	78,616,000	78,616,000
B.	Groups 1-4, Total Unit Sales, 2001 - 2002	93,720,000	93,720,000	93,720,000
C.	Group 1, Share of Total Unit Sales, 2001 - 2002 (A/B)	83.9 %	83.9 %	83.9 %
D.	Estimated Annual Unit Demand[2]	50,000,000	50,000,000	50,000,000
E.	Group 1, Estimated Annual Unit Sales (CxD)	41,950,000	41,950,000	41,950,000
F.	Share of Group 1 Sales[3]	13.3 %	14.9 %	71.8 %
G.	Estimated Annual Unit Sales (ExF)	5,579,350	6,250,550	30,120,100
H.	Group 1, Share of Unit Sales for Brand albuterol MDIs, 2001-2002	11.9 %	11.9 %	11.9 %
I.	Group 1, Share of Unit Sales for Generic albuterol MDIs, 2001-2002	88.1 %	88.1 %	88.1 %
J.	Estimated Annual Brand Unit Sales (GxH)	663,943	743,815	3,584,292
K.	Estimated Annual Generic Unit Sales (GxI)	4,915,407	5,506,735	26,535,808
L.	Group 1, Weighted Average Retailers' Acquisition Costs for Brand albuterol MDIs, 2001-2002[4]	$ 26.82	$ 26.82	$ 26.82
M.	Group 1, Weighted Average Retailers' Acquisition Costs for Generic albuterol MDIs, 2001-2002	$ 5.68	$ 5.68	$ 5.68

ESTIMATED ANNUAL WHOLESALERS' AND MANUFACTURERS' REVENUES FOR SALES OF BRAND AND GENERIC ALBUTEROL MDIs TO CASH, MEDICAID, AND INSURANCE PAYERS THROUGH GROUP 1 CHANNELS[1]

		Cash Payers (1)	Medicaid Payers (2)	Insurance Payers (3)
N.	Estimated Annual Wholesalers' Revenues for Brand albuterol MDIs (JxL)	$ 17,806,951	$ 19,949,118	$ 96,130,711
O.	Estimated Annual Wholesalers' Revenues for Generic albuterol MDIs (KxM)	$ 27,919,512	$ 31,278,255	$ 150,723,389
P.	Estimated Annual **Wholesalers' Revenues** for Brand and Generic albuterol MDIs (N+O)	$ 45,726,463	$ 51,227,373	$ 246,854,100
Q.	Estimated Annual Manufacturers' Gross Revenues for Brand albuterol MDIs (Nx96%)[5]	$ 17,094,673	$ 19,151,153	$ 92,285,483
R.	Estimated Annual Manufacturers' Gross Revenues for Generic albuterol MDIs (Ox96%)[5]	$ 26,802,732	$ 30,027,125	$ 144,694,453
S.	Estimated Annual **Manufacturers' Gross Revenues** for Brand and Generic albuterol MDIs (Q+R)	$ 43,897,405	$ 49,178,278	$ 236,979,936
T.	Percentage Manufacturers' Rebates for Brand albuterol MDIs[6]	- %	30.0 %	15.1 %
U.	Percentage Manufacturers' Rebates for Generic albuterol MDIs[7]	- %	11.0 %	- %
V.	Annual Manufacturers' Rebates for Brand albuterol MDIs (QxT)	$ -	$ 5,745,346	$ 13,935,108
W.	Annual Manufacturers' Rebates for Generic albuterol MDIs (RxU)	$ -	$ 3,302,984	$ -
X.	Annual Manufacturers' Rebates for Brand and Generic albuterol MDIs (V+W)	$ -	$ 9,048,330	$ 13,935,108

ESTIMATED ANNUAL WHOLESALERS' AND MANUFACTURERS' REVENUES FOR SALES OF BRAND AND GENERIC ALBUTEROL MDIs TO CASH, MEDICAID, AND INSURANCE PAYERS THROUGH GROUP 1 CHANNELS[1]

		Cash Payers (1)	Medicaid Payers (2)	Insurance Payers (3)
Y.	Estimated Annual Manufacturers' Revenues for Brand albuterol MDIs, Net of Rebates (Q-V)	$ 17,094,673	$ 13,405,807	$ 78,350,375
Z.	Estimated Annual Manufacturers' Revenues for Generic albuterol MDIs, Net of Rebates (R-W)	$ 26,802,732	$ 26,724,141	$ 144,694,453
AA.	Estimated Annual **Manufacturers' Revenues** for Brand and Generic albuterol MDIs, **Net of Rebates** (Y+Z)	$ 43,897,405	$ 40,129,948	$ 223,044,828

- not applicable

[1] Group 1 channels include chain stores, independent stores, mail order, food stores, long-term care, home healthcare, and miscellaneous - other.

[2] Based on IMS data analysis of total annual unit sales from 1992 to 2002.

[3] Based on the combined share of total prescription unit sales in 2001 and 2002 of albuterol MDIs to Cash, Medicaid, and Third-Party Payers as reported by Verispan, SPA.

[4] Equal to the sum of the total revenue for brand albuterol MDI products (Ventolin CFC, Ventolin HFA, Proventil CFC, and Proventil HFA) in 2001 and 2002 divided by the sum of the total units sold for brand albuterol MDIs products in 2001 and 2002.

[5] The National Association of Chain Drugs Stores reported that for the average retail prescription cost in 2002, the manufacturer and wholesaler received 75.6% and 3.3% of the cost, respectively. IMS data reported sales at the wholesaler level. Thus, the total IMS wholesaler revenue represents 78.9% (75.6%+3.3%) of the total cost. The revenue due the manufacturer is 96% of the total amount reported by IMS (75.6%/78.9%).

[6] Assume Cash Payers receive no manufacturer rebates. Rebates to Insurance and Medicaid Payers are based on typical manufacturer rebates for branded product. OBRA 90 provides that manufacturers of branded pharmaceuticals pay a minimum rebate of 15.1 percent on the wholesale price on branded products dispensed to outpatients covered by Medicaid. Medicaid receives larger rebates if manufacturers offer lower prices to any other purchasers in the U.S.

[7] OBRA 90 provides that manufacturers of generic pharmaceuticals pay a minimum rebate of 11.0 percent on the wholesale price on generic products dispensed to outpatients covered by Medicaid.

Source: IMS data; Verispan, SPA data; "Industry Statistics, Industry Facts-at-a-Glance, Pharmaceutical Pricing," National Association of Chain Drug Stores, http://www.nacds.org/wmspage.cfm?parm1=507; "Prescription Drugs, Expanding Access to Federal Prices Could Cause Other Changes," U.S. General Accounting Office, GAO/HEHS-00-118, August 2000; and William von Oehsen, "Pharmaceutical Discounts under Federal Law: State Program Opportunities," speech at the National Conference of State Legislatures Fifth Health Policy Conference, November 16, 2001.

ESTIMATED ANNUAL RETAILERS' REVENUES AND COSTS TO PATIENTS AND THIRD-PARTY PAYERS FOR SALES OF BRAND AND GENERIC ALBUTEROL MDIs TO CASH, MEDICAID, AND INSURANCE PAYERS THROUGH GROUP 1 CHANNELS[1]

		Cash Payers (1)	Medicaid Payers (2)	Insurance Payers (3)
A.	Group 1, Weighted Average Retailers' Acquisition Costs for Brand albuterol MDIs, 2001-2002[2]	$ 26.82	$ 26.82	$ 26.82
B.	Group 1, Weighted Average Retailers' Acquisition Costs for Generic albuterol MDIs, 2001-2002	$ 5.68	$ 5.68	$ 5.68
C.	Estimated Retailers' Mark-ups on Brand albuterol MDIs[3]	28.8 %	28.8 %	14.4 %
D.	Estimated Retailers' Mark-ups on Generic albuterol MDIs[4]	363.3 %	234.5 %	234.5 %
E.	Retail Prices for Brand albuterol MDIs [A+(AxC)]	$ 34.54	$ 34.54	$ 30.68
F.	Retail Prices for Generic albuterol MDIs [B+(BxD)]	$ 26.32	$ 19.00	$ 19.00
G.	Estimated Annual Brand Unit Sales	663,943	743,815	3,584,292
H.	Estimated Annual Generic Unit Sales	4,915,407	5,506,735	26,535,808
I.	Estimated Annual Retailers' Revenues for Brand albuterol MDIs (ExG)	$ 22,932,591	$ 25,691,370	$ 109,966,079
J.	Estimated Annual Retailers' Revenues for Generic albuterol MDIs (FxH)	$ 129,373,512	$ 104,627,965	$ 504,180,352
K.	Estimated Annual **Retailers' Revenues** for Brand and Generic albuterol MDIs (I+J)	$ 152,306,103	$ 130,319,335	$ 614,146,431
L.	Annual Manufacturers' Rebates for Brand and Generic albuterol MDIs	$ -	$ 9,048,330	$ 13,935,108

ESTIMATED ANNUAL RETAILERS' REVENUES AND COSTS TO PATIENTS AND THIRD-PARTY PAYERS FOR SALES OF BRAND AND GENERIC ALBUTEROL MDIs TO CASH, MEDICAID, AND INSURANCE PAYERS THROUGH GROUP 1 CHANNELS[1]

	Cash Payers (1)	Medicaid Payers (2)	Insurance Payers (3)
M. Annual Total Costs borne by Patients and Third-Party Payers (K-L)	$ 152,306,103	$ 121,271,005	$ 600,211,323
N. **Annual Costs to Patients**[5]	$ 152,306,103	$ -	$ 344,212,504
O. **Annual Costs to Third-Party Payers** (M-N)	$ -	$ 121,271,005	$ 255,998,819

- not applicable

[1] Group 1 channels include chain stores, independent stores, mail order, food stores, long-term care, home healthcare, and miscellaneous - other.

[2] Equal to the sum of the total revenue for brand albuterol MDI products (Ventolin CFC, Ventolin HFA, Proventil CFC, and Proventil HFA) in 2001 and 2002 divided by the sum of the total units sold for brand albuterol MDIs products in 2001 and 2002.

[3] Based on the weighted average price for brand albuterol MDIs to chain stores, food stores, and independent stores of $29.99 for the period May 2002 to February 2003, derived from IMS data, and the average retail price of $38.62 for the period May 2002 to April 2003 for the same channels, Verispan, SPA data. The retailer mark-up is equal to the average retail price of $38.62 less the average retail acquisition cost of $29.99, divided by the average retail acquisition cost or 28.8%. We assumed Insurance Payers negotiated a 50% discount on the retailer mark-up.

[4] Based on the weighted average price for generic albuterol MDIs to chain stores, food stores, and independent stores of $4.88 for the period May 2002 to February 2003, derived from IMS data, and the average retail price of $22.61 for the period May 2002 to April 2003 for the same channels, Verispan data. The retailer mark-up is equal to the average retail price of $22.61 less the average retail acquisition cost of $4.88, divided by the average retail acquisition cost or 363.3%. The retailer mark-up to Medicaid of 234.5% is based on a Federal Maximum Allowable Cost or MAC, which includes a dispensing fee of $19. We assumed Insurance Payers negotiated a discount similar to Medicaid.

[5] Assumes Patients that are Cash Payers receive no assistance. We understand Patients with Medicaid coverage receive pharmaceutical products at no cost. Assumes Patients with Insurance Coverage pay a copayment of $22 and $10 for brand and generic albuterol MDIs, respectively, based on the estimated average copayment in 2003 reported in "Strategic Health Plans Update 2002" by *Health Strategies Group*.

Source: IMS data; Verispan, SPA data; "Strategic Health Plans Update 2002," *Health Strategies Group*; "Prescription Drugs, Expanding Access to Federal Prices Could Cause Other Changes," U.S. General Accounting Office, GAO/HEHS-00-118, August 2000; William von Oehsen, "Pharmaceutical Discounts under Federal Law: State Program Opportunities," speech at the National Conference of State Legislatures Fifth Health Policy Conference, November 16, 2001; NERA table, "Estimated Annual Wholesalers' and Manufacturers' Revenues for Sales of Brand and Generic Albuterol MDIs to Cash, Medicaid, and Insurance Payers through Group 1 Channels"; and information provided by GSK.

ESTIMATED ANNUAL WHOLESALERS' AND MANUFACTURERS' REVENUES FOR SALES OF BRAND HFA ALBUTEROL MDIs TO CASH, MEDICAID, AND INSURANCE PAYERS THROUGH GROUP 1 CHANNELS[1]

ASSUMES FDA DESIGNATES ALBUTEROL NON-ESSENTIAL

		Cash Payers (1)	Medicaid Payers (2)	Insurance Payers (3)
A.	Group 1, Total Unit Sales, 2001 - 2002	78,616,000	78,616,000	78,616,000
B.	Groups 1-4, Total Unit Sales, 2001 - 2002	93,720,000	93,720,000	93,720,000
C.	Group 1, Share of Total Unit Sales, 2001 - 2002 (A/B)	83.9 %	83.9 %	83.9 %
D.	Estimated Annual Unit Demand[2]	50,000,000	50,000,000	50,000,000
E.	Group 1, Estimated Annual Unit Sales (CxD)	41,950,000	41,950,000	41,950,000
F.	Share of Group 1 Sales[3]	13.3 %	14.9 %	71.8 %
G.	Estimated Annual Unit Sales (ExF)	5,579,350	6,250,550	30,120,100
H.	Group 1, Weighted Average Retailers' Acquisition Costs for Brand HFA albuterol MDIs, 2001-2002	$ 27.88	$ 27.88	$ 27.88
I.	Estimated Annual **Wholesalers' Revenues** for Brand HFA albuterol MDIs (GxH)	$ 155,552,278	$ 174,265,334	$ 839,748,388
J.	Estimated Annual **Manufacturers' Gross Revenues** for Brand HFA albuterol MDIs (Ix96%)[4]	$ 149,330,187	$ 167,294,721	$ 806,158,452
K.	Percentage Manufacturers' Rebates for Brand HFA albuterol MDIs[5]	- %	15.1 %	15.1 %
L.	Annual Manufacturers' Rebates for Brand HFA albuterol MDIs (JxK)	$ -	$ 25,261,503	$ 121,729,926

ESTIMATED ANNUAL WHOLESALERS' AND MANUFACTURERS' REVENUES FOR SALES OF BRAND HFA ALBUTEROL MDIs TO CASH, MEDICAID, AND INSURANCE PAYERS THROUGH GROUP 1 CHANNELS[1]

ASSUMES FDA DESIGNATES ALBUTEROL NON-ESSENTIAL

	Cash Payers (1)	Medicaid Payers (2)	Insurance Payers (3)
M. Estimated Annual **Manufacturers' Revenues** for Brand HFA albuterol MDIs, **Net of Rebates** (J-L)	$ 149,330,187	$ 142,033,218	$ 684,428,526

- not applicable

[1] Group 1 channels include chain stores, independent stores, mail order, food stores, long-term care, home healthcare, and miscellaneous - other.

[2] Based on IMS data analysis of total annual unit sales from 1992 to 2002.

[3] Based on the combined share of total prescription unit sales in 2001 and 2002 of albuterol MDIs to Cash, Medicaid, and Third-Party Payers as reported by Verispan, SPA.

[4] The National Association of Chain Drugs Stores reported that for the average retail prescription cost in 2002, the manufacturer and wholesaler received 75.6% and 3.3% of the cost, respectively. IMS data reported sales at the wholesaler level. Thus, the total IMS wholesaler revenue represents 78.9% (75.6%+3.3%) of the total cost. The revenue due the manufacturer is 96% of the total amount reported by IMS (75.6%/78.9%).

[5] Assume Cash Payers receive no manufacturer rebates. Rebates to Insurance and Medicaid Payers are based on typical manufacturer rebates for branded product. OBRA 90 provides that manufacturers of branded pharmaceuticals pay a minimum rebate of 15.1 percent on the wholesale price on branded products dispensed to outpatients covered by Medicaid. Medicaid receives larger rebates if manufacturers offer lower prices to any other purchasers in the U.S.

Source: IMS data; Verispan, SPA data; "Industry Statistics, Industry Facts-at-a-Glance, Pharmaceutical Pricing," National Association of Chain Drug Stores, http://www.nacds.org/wmspage.cfm?parm1=507; "Prescription Drugs, Expanding Access to Federal Prices Could Cause Other Changes," U.S. General Accounting Office, GAO/HEHS-00-118, August 2000; and William von Oehsen, "Pharmaceutical Discounts under Federal Law: State Program Opportunities," speech at the National Conference of State Legislatures Fifth Health Policy Conference, November 16, 2001.

ESTIMATED ANNUAL RETAILERS' REVENUES AND COSTS TO PATIENTS AND THIRD-PARTY PAYERS FOR SALES OF BRAND HFA ALBUTEROL MDIs TO CASH, MEDICAID, AND INSURANCE PAYERS THROUGH GROUP 1 CHANNELS[1]

ASSUMES FDA DESIGNATES ALBUTEROL NON-ESSENTIAL

		Cash Payers (1)	Medicaid Payers (2)	Insurance Payers (3)
A.	Group 1, Weighted Average Retailers' Acquisition Costs for Brand HFA albuterol MDIs, 2001-2002	$ 27.88	$ 27.88	$ 27.88
B.	Estimated Retailers' Mark-ups on Brand HFA albuterol MDIs[2]	28.8 %	28.8 %	14.4 %
C.	Retail Prices for Brand HFA albuterol MDIs [A+(AxB)]	$ 35.91	$ 35.91	$ 31.89
D.	Estimated Annual Unit Sales	5,579,350	6,250,550	30,120,100
E.	Estimated Annual **Retailers' Revenues** for Brand HFA albuterol MDIs (CxD)	$ 200,354,459	$ 224,457,251	$ 960,529,989
F.	Annual Manufacturers' Rebates for Brand HFA albuterol MDIs	$ -	$ 25,261,503	$ 121,729,926
G.	Annual Total Costs borne by Patients and Third-Party Payers (E-F)	$ 200,354,459	$ 199,195,748	$ 838,800,063
H.	**Annual Costs to Patients**[3]	$ 200,354,459	$ -	$ 662,642,200
I.	**Annual Costs to Third-Party Payers** (G-H)	$ -	$ 199,195,748	$ 176,157,863

- not applicable

ESTIMATED ANNUAL RETAILERS' REVENUES AND COSTS TO PATIENTS AND THIRD-PARTY PAYERS FOR SALES OF BRAND HFA ALBUTEROL MDIs TO CASH, MEDICAID, AND INSURANCE PAYERS THROUGH GROUP 1 CHANNELS[1]

ASSUMES FDA DESIGNATES ALBUTEROL NON-ESSENTIAL

[1] Group 1 channels include chain stores, independent stores, mail order, food stores, long-term care, home healthcare, and miscellaneous - other.

[2] Based on the weighted average price for brand albuterol MDIs to chain stores, food stores, and independent stores of $29.99 for the period May 2002 to February 2003, derived from IMS data, and the average retail price of $38.62 for the period May 2002 to April 2003 for the same channels, Verispan, SPA data. The retailer mark-up is equal to the average retail price of $38.62 less the average retail acquisition cost of $29.99, divided by the average retail acquisition cost or 28.8%. We assumed Insurance Payers negotiated a 50 percent discount on the retailer mark-up.

[3] Assumes Patients that are Cash Payers receive no assistance. We understand Patients with Medicaid coverage receive pharmaceutical products at no cost. Assumes Patients with Insurance Coverage pay a copayment of $22 for brand HFA albuterol MDIs, based on the estimated average copayment in 2003 reported in "Strategic Health Plans Update 2002" by *Health Strategies Group*.

Source: IMS data; Verispan, SPA data; "Strategic Health Plans Update 2002," *Health Strategies Group*; and NERA table, "Estimated Annual Wholesalers' and Manufacturers' Revenues for Sales of Brand HFA Albuterol MDIs to Cash, Medicaid, and Insurance Payers through Group 1 Channels, Assumes FDA Designates Albuterol Non-Essential."

ESTIMATED ANNUAL WHOLESALERS' AND MANUFACTURERS' REVENUES AND COSTS TO PATIENTS AND THIRD-PARTY PAYERS FOR SALES OF BRAND AND GENERIC ALBUTEROL MDIs THROUGH GROUPS 2, 3, AND 4[1]

		Group 2 (1)	Group 3 (2)	Group 4 (3)
A.	Total Unit Sales, 2001 - 2002	4,046,000	5,633,000	5,425,000
B.	Groups 1-4, Total Unit Sales, 2001 - 2002	93,720,000	93,720,000	93,720,000
C.	Share of Total Unit Sales, 2001 - 2002 (A/B)	4.3 %	6.0 %	5.8 %
D.	Estimated Annual Unit Demand[2]	50,000,000	50,000,000	50,000,000
E.	Estimated Annual Unit Sales (CxD)	2,150,000	3,000,000	2,900,000
F.	Share of Unit Sales for Brand albuterol MDIs, 2001-2002	26.0 %	48.0 %	20.1 %
G.	Share of Unit Sales for Generic albuterol MDIs, 2001-2002	74.0 %	52.0 %	79.9 %
H.	Estimated Annual Brand Unit Sales (ExF)	559,000	1,440,000	582,900
I.	Estimated Annual Generic Unit Sales (ExG)	1,591,000	1,560,000	2,317,100
J.	Weighted Average Acquisition Costs for Brand albuterol MDIs, 2001-2002[3]	$ 14.44	$ 10.04	$ 8.22
K.	Weighted Average Acquisition Costs for Generic albuterol MDIs, 2001-2002	$ 3.34	$ 4.78	$ 2.08
L.	Estimated Annual Wholesalers' Revenues for Brand albuterol MDIs (HxJ)	$ 8,071,960	$ 14,457,600	$ 4,791,438
M.	Estimated Annual Wholesalers' Revenues for Generic albuterol MDIs (IxK)	$ 5,313,940	$ 7,456,800	$ 4,819,568
N.	Estimated Annual **Wholesalers' Revenues** for Brand and Generic albuterol MDIs (L+M)	$ 13,385,900	$ 21,914,400	$ 9,611,006

ESTIMATED ANNUAL WHOLESALERS' AND MANUFACTURERS' REVENUES AND COSTS TO PATIENTS AND THIRD-PARTY PAYERS FOR SALES OF BRAND AND GENERIC ALBUTEROL MDIs THROUGH GROUPS 2, 3, AND 4[1]

	Group 2 (1)	Group 3 (2)	Group 4 (3)
O. Estimated Annual Manufacturers' Revenues for Brand albuterol MDIs (Lx96%)[4]	$ 7,749,082	$ 13,879,296	$ 4,599,780
P. Estimated Annual Manufacturers' Revenues for Generic albuterol MDIs (Mx96%)[4]	$ 5,101,382	$ 7,158,528	$ 4,626,785
Q. Estimated Annual **Manufacturers' Revenues** for Brand and Generic albuterol MDIs (O+P)	$ 12,850,464	$ 21,037,824	$ 9,226,565
R. **Annual Costs to Patients**[5]	$ 10,750,000	$ -	$ -
S. **Annual Costs to Third-Party Payers** (N-R)	$ 2,635,900	$ 21,914,400	$ 9,611,006

- not applicable

[1] Group 2 channels include clinics, HMOs, and universities; Group 3 channels include non-federal hospitals; and Group 4 channels include federal facilities and prisons.

[2] Based on IMS data analysis of total annual unit sales from 1992 to 2002.

[3] Equal to the sum of the total revenue for brand albuterol MDI products (Ventolin CFC, Ventolin HFA, Proventil CFC, and Proventil HFA) in 2001 and 2002 divided by the sum of the total units sold for brand albuterol MDIs products in 2001 and 2002 for each Group.

[4] The National Association of Chain Drugs Stores reported that for the average retail prescription cost in 2002, the manufacturer and wholesaler received 75.6% and 3.3% of the cost, respectively. IMS data reported sales at the wholesaler level. Thus, the total IMS wholesaler revenue represents 78.9% (75.6%+3.3%) of the total cost. The revenue due the manufacturer is 96% of the total amount reported by IMS (75.6%/78.9%).

[5] Assume Patients through Group 2 channels pay a copayment of $5 for brand and generic albuterol MDIs.

Source: IMS data; "Industry Statistics, Industry Facts-at-a-Glance, Pharmaceutical Pricing," National Association of Chain Drug Stores, http://www.nacds.org/wmspage.cfm?parm1=507; and information provided by GSK.

ESTIMATED ANNUAL WHOLESALERS' AND MANUFACTURERS' REVENUES AND COSTS TO PATIENTS AND THIRD-PARTY PAYERS FOR SALES OF BRAND HFA ALBUTEROL MDIs THROUGH GROUPS 2, 3, AND 4[1]

ASSUMES FDA DESIGNATES ALBUTEROL NON-ESSENTIAL

	Group 2 (1)	Group 3 (2)	Group 4 (3)
A. Total Unit Sales, 2001 - 2002	4,046,000	5,633,000	5,425,000
B. Groups 1-4, Total Unit Sales, 2001 - 2002	93,720,000	93,720,000	93,720,000
C. Share of Total Unit Sales, 2001 - 2002 (A/B)	4.3 %	6.0 %	5.8 %
D. Estimated Annual Unit Demand[2]	50,000,000	50,000,000	50,000,000
E. Estimated Annual Unit Sales (CxD)	2,150,000	3,000,000	2,900,000
F. Weighted Average Acquisition Costs for Brand HFA albuterol MDIs, 2001-2002	$ 24.14	$ 22.68	$ 18.64
G. Estimated Annual **Wholesalers' Revenues** for Brand HFA albuterol MDIs (ExF)	$ 51,901,000	$ 68,040,000	$ 54,056,000
H. Estimated Annual **Manufacturers' Revenues** for Brand HFA albuterol MDIs (Gx96%)[3]	$ 49,824,960	$ 65,318,400	$ 51,893,760
I. **Annual Costs to Patients**[4]	$ 10,750,000	$ -	$ -
J. **Annual Costs to Third-Party Payer** (G-I)	$ 41,151,000	$ 68,040,000	$ 54,056,000

- not applicable

ESTIMATED ANNUAL WHOLESALERS' AND MANUFACTURERS' REVENUES AND COSTS TO PATIENTS AND THIRD-PARTY PAYERS FOR SALES OF BRAND HFA ALBUTEROL MDIs THROUGH GROUPS 2, 3, AND 4[1]

ASSUMES FDA DESIGNATES ALBUTEROL NON-ESSENTIAL

[1] Group 2 channels include clinics, HMOs, and universities; Group 3 channels include non-federal hospitals; and Group 4 channels include federal facilities and prisons.

[2] Based on IMS data analysis of total annual unit sales from 1992 to 2002.

[3] The National Association of Chain Drugs Stores reports that for the average retail prescription cost in 2002, the manufacturer and wholesaler received 75.6% and 3.3% of the cost, respectively. IMS data reports sales at the wholesaler level. Thus, the total IMS wholesaler revenue represents 78.9% (75.6%+3.3%) of the total cost. The revenue due the manufacturer is 96% of the total amount reported by IMS (75.6%/78.9%).

[4] Assume Patients through Group 2 channels pay a copayment of $5 for brand albuterol MDIs.

Source: IMS data; "Industry Statistics, Industry Facts-at-a-Glance, Pharmaceutical Pricing," National Association of Chain Drug Stores, http://www.nacds.org/wmspage.cfm?parm1=507; and information provided by GSK.